

MEDICINE

HANDWRITTEN NOTE

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Name :

Subject :

Medicine

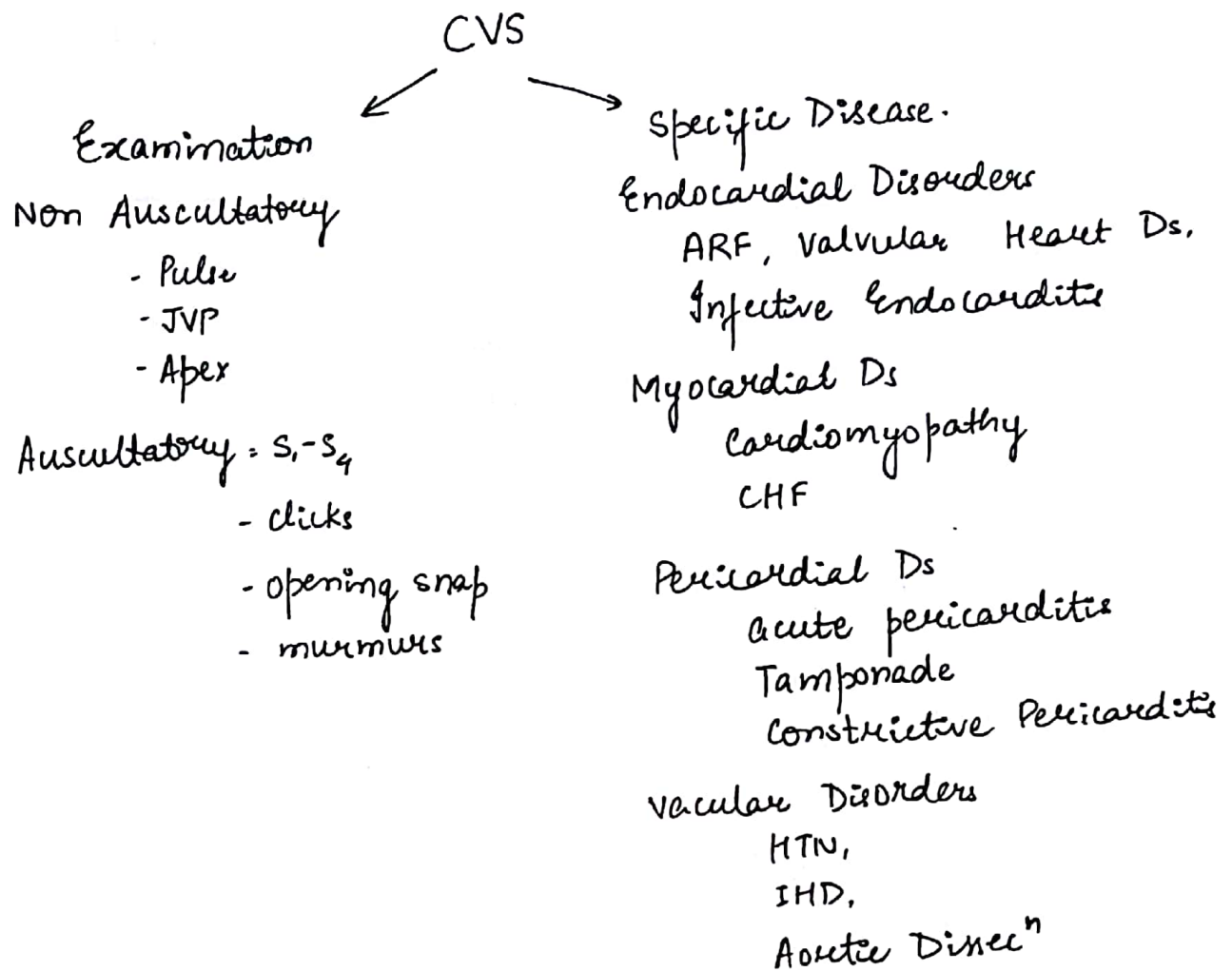


CVS

RHEUMATOLOGY

RESPIRATORY

ACID - BASE BALANCE



PULSE

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(I) Pulse Rate

(N) 60 - 100/min

Ab (N)

1) Bradycardia - < 60/min.

Causes

Physiological

- 1) Elderly
(age related SA node degeneration)
- 2) Sleep
(↓ in sympathetic activity)
- 3) Athletes
(Basal ↑ in vagal D/c)

(N) Thyroid hormone
↑ No. + ↑ funcⁿ of β_1 receptors

To perfuse brain systemic
BP ↑ → stimulate baro
receptors in carotid
↓
release vagal D/c

Pathological

I) CVS Cause

- 1) Bradycardias
(AV Block)
- 2) MI [inf. wall]
SA node also supplied by
② coronary artery
due to stimulation
of vagal n/v nearby

II) Non-CVS Causes

- 1) Hypothyroidism
- 2) Hypothermia
(directly affects SA Node)
- 3) Drugs
 - a) β blocker
 - b) non DHP-CCB [cause AV Block]
 - c) ~~Digoxin~~ Digoxin. effect

4) ↑ ICP
Cushing's reflex = BP ↑, HR ↓,
irregular resp

↑ Bile ⇒ ⊖ SA node

⑤ Obstructive jaundice

2) **Tachycardia** > 100/min

CAUSES

Physiological

- 1) Infants (↑ SA node activity)
- 2) Anxiety (↑ sympathetic activity)
- 3) Exercise (↑ demand)

Sympathetic system ← Thoracic n/vs
[thoracolumbar]

Pathological

I CVS causes

- 1) Tachy ~~arrhythmias~~ ^{arrhythmias} ~~brady~~ ^{brachycardias}
 - a) PSVT
 - b) AF

2) MI (ant. wall)

← [stimulation of nearby sympathetic n/vs]

II Non-CVS causes

1) Hyperthyroidism.

2) Fever.

3) Beta-Beta

4) Drugs

a) β agonist

b) short acting DHPs [reflex tachycardia due to compensation]

c) Digoxin toxicity

d) Theophyllin

e) Thyroxin.

③ Relative Bradycardia / FAHET'S SIGN Q,

HR doesn't ↑ in proportion to body temperature.

④ For every 1°C from 37°C .

↓
HR ↑ by 15-20/min from baseline

For every 1°F from 98°F → HR ↑ by 10/min.

E.g. if Body Temp is 40°C . HR = 112/min (baseline = 80/min)
min expected HR = $80 + 45$
= 125.

CAUSES

Infectious

(also ⊖ SA node)

- 1) Typhoid fever
- 2) Brucella
- 3) Legionella
(sputum AFB +ve)
- 4) Viral

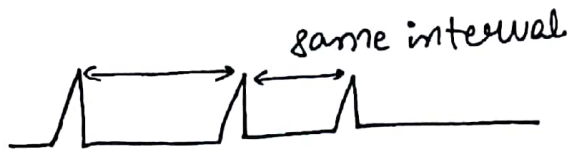
Non-Infectious

- 1) Drug induced fever
- 2) Self induced fever or
Factitious Fever Q.
- 3) Fraudulent Fever
(thermometer only).

② Rhythm :-

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① → Regular = Fixed interval b/w any 2 consecutive pulses



Ab ①

Physiological

Pathological.

Sinus arrhythmia

HR changes \pm inspiration & expiration

During Inspiratory Phase

(-ve) Intrathoracic Pressure

↑ Blood flow into R side of heart

Pulmonary vessels dilatation
(blood pooling)

↓ blood flow into L side of heart

CO will ↓

SBP will ↓

Baroreceptor stimulation ↓

vagal release ↓

HR ~~↓~~ ↑

During Expiratory Phase.

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(+) Intrathoracic Pressure

↓
↓ blood flow into R side of heart

↑
Pulmonary vessels are squeezed

↓
↑ blood flow into L side of heart

↓
CO will (↑)

↓
SBP (↑)

↓
Baroreceptor (+) ↑

↓
Vagal (↑)

↓
HR (↓)

Pathological

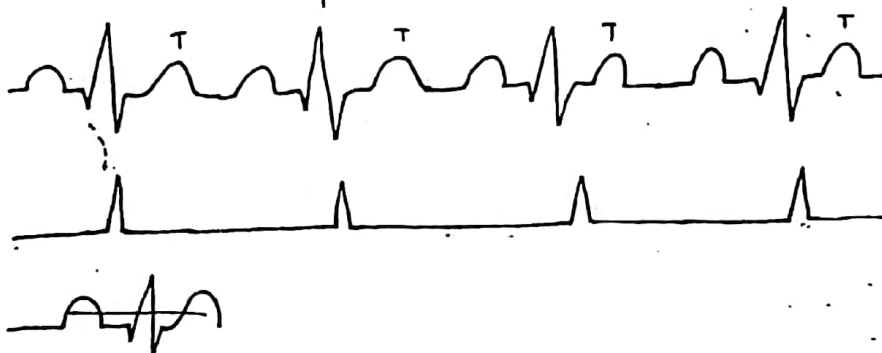
I) Regularly irregular rhythm
↓ ↓
predictable variable.

CAUSE :-

1) Bigeminy Rhythm ← Digoxin Toxicity

every alternate ventricle contraction + depolarization is due to premature ventricle ectopic

(N) ECG.



Pulse

Bigemy



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premature ventricular ectopic [wide p, QRS prolonged, inverted T. due to abnormal depolarisation]

Pulse Bigeminus



↑ due to ectopic.

↓ amplitude due to ↓ ventricle filling time hence ↓ stroke volume

II Irregularly Irregular rhythm

no predictable variation in intervals.

CAUSE = Atrial fibrillation. = variable HR

III PULSE PRESSURE.

How well a ^{pulse is} felt

(N) = SBP - DBP [30 - 60 mm Hg].

Ab(N)

↓ PP. / Thready Pulse.

Mech. if SBP ↓ & DBP ↑

if CO ↓

↓
stimulate sympathetic activity

↓
arteriolar constriction



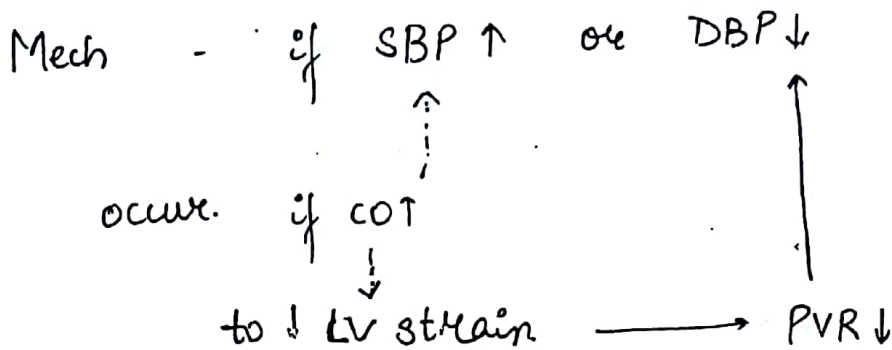
PVR ↑

CAUSE = Shock [Hypovolemia, shock].

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not found in septic or neurogenic shock.

II> ↑ PP / Bounding Pulse.



CO is inversely related to PVR

CAUSE: 1) ↑ CO state

CVS

- 1) AR
- 2) MR.
- 3) PDA

Non-CVS

Physiological → ⊕
when plasma vol ↑

Pathological →

1) Hyperthyroidism

β₁ rec ⊕

inotropic

↓

CO ↑ = ↑ SV

X

chronotropic

↓

HR ↑

Ⓝ vit B₁ ⊖ NO synthase

if Def of vit B₁
↳ vasodilatation

↓ PVR ↓ → CO ↑

2) Anaemia

3) Bere-Bere

PVR ↓ as
arterioles are
bypassed

↳ CO ↑

4) A-V fistula

5) Paget's Disease

[A-V fistula in Bone]

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Q. \subseteq low CO state will cause bounding pulse?

Ans. severe bradycardia \subseteq complete AV Block

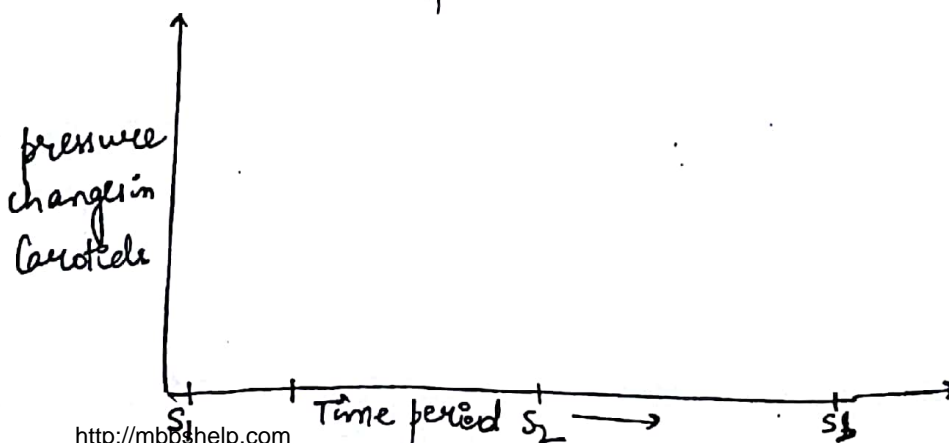
SV ↑ \times HR ↓↓ \rightarrow CO ↓

AV Block \rightarrow ↓ depolarisation of ~~pacemaker~~ Purkinje
fibres
 \downarrow
Rate ↓ [propag speed is less in AVN]
 \downarrow
But EDV ↑
 \downarrow
SV ↑

(W) CHARACTER

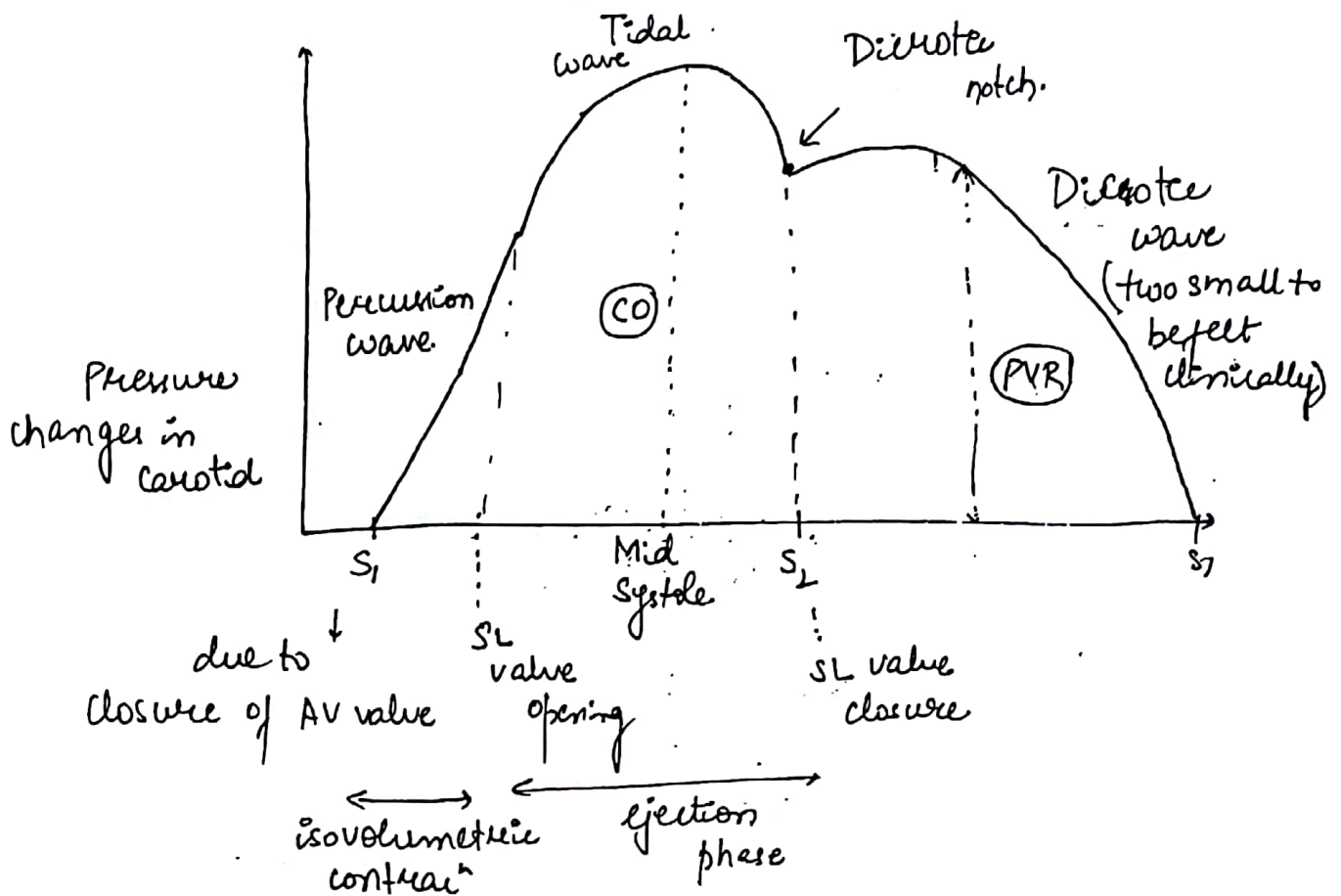
Rate	Rhythm	best ausculted in	Radial artery
Character / contour	"	"	Carotid artery

(N) Waveforms of Carotid.



S_1 is due to closure of AV valves

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WAVE

① Pericardial wave

It is due to pressure transmission by isovolumetric LV contraction onto carotids.

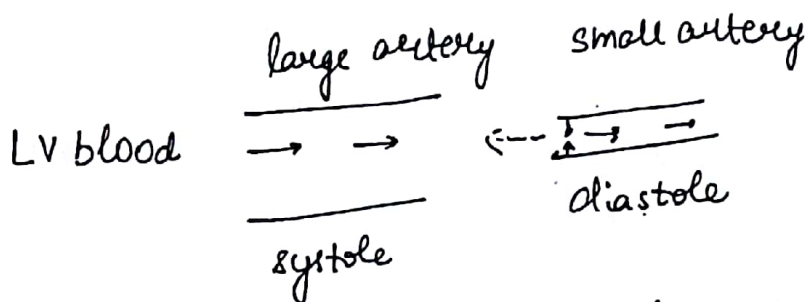
② Tidal wave

Beating of blood ejected into carotid ring, its pressure further.

③ Dicrotic wave

Due to back pressure reflection from small vessels.

Dicrotic notch represents closure of aortic, pulmonary valve (S_2)



Recoil of small vessel leads to +ve pressure impulse

Ab (N)

1) Hyperkinetic Pulse

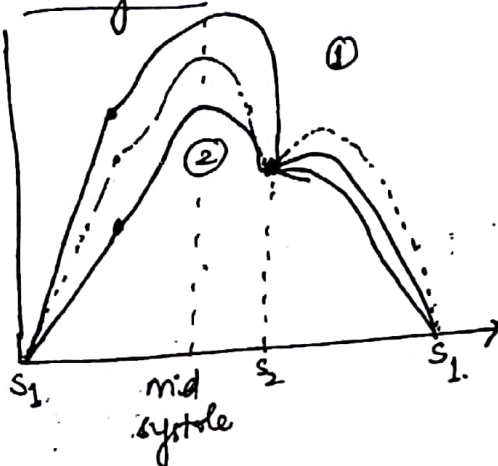
⇒ ↑ amplitude

Diagram

Diastole

Cause

↑ CO state



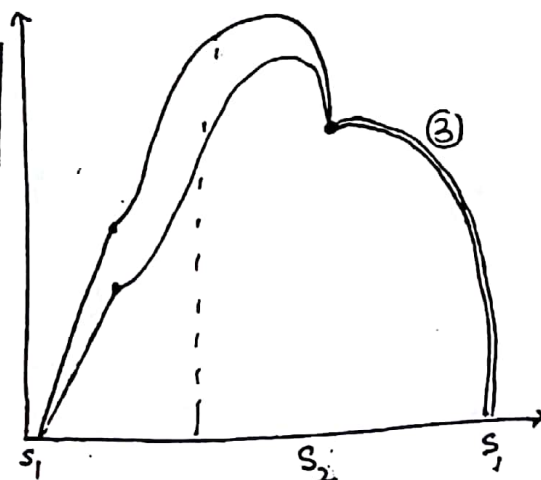
2) Hypokinetic Pulse

⇒ ↓ amplitude

though diastolic wave is ① but still not felt not felt clinically.

↓ CO state

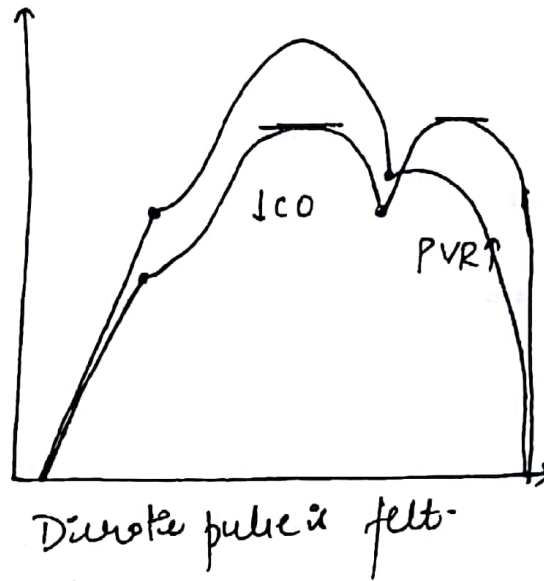
3) ↓ amplitude: Pulsus late peak = et tardus



most specific pulse of severe AS.

④ Divotic Pulse

= 2 peaks
one in systole
other in diastole

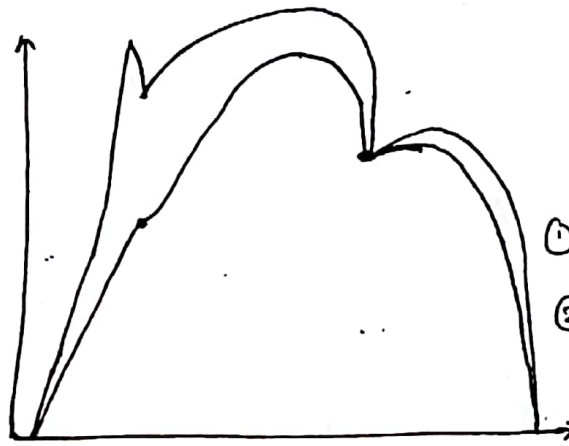


Shock
(Hypovolaemic
Cardiogenic)

⑤ Bifidens Pulse

= 2 peaks
③ in systole

Best assessed in
Peripheral artery



- ① Severe AR.
- ② Severe AR + AS

Brisk isovolumetric
ventricular contraction

(↑ LV vol. + ↑ stretching)

↓
Percussion wave will shift to ④
(as duration is less)

↓
gets separated from tidal
wave

It will make
tidal wave to
come late.

③ HOCM --- ?

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↳ PULSUS ALTERNANS - Best assessed in Radial.

Regular alteration of pulse amplitude.



only amplitude changes, interval remain same
most specific pulse.

CAUSE → LV (systolic) Dysfuncⁿ.

✓ most specific pulse.

2) PULSE DEFICIT :-

PULSE DEFICIT :-

(N) HR - PR ← due to adequate SV = 0
↳ arterial pulsation is felt

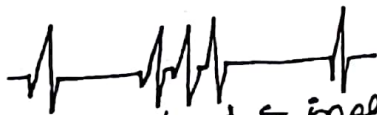
↓
due to ventricle
contraction


Ab(N) if $HR - PR = (+ve) \Rightarrow$ ~~Pulse~~ DEFICIT.

CAUSES

CAUSES

1) AF \bar{c} variable heart rate




 ECG tracing showing inadequate ventricular filling. The top trace shows a narrow QRS complex with a small R wave and a deep S wave, labeled "inadequate ventricular filling". The bottom trace shows a normal QRS complex with a tall R wave and a small S wave, labeled "adequate ventricular filling".

Here 5 HR but 3 PR

2) Premature Ventricle Ectopics

less filling time \rightarrow pulse not felt

If pulse Deficit $> +10/\text{min} \Rightarrow \text{AF only}$

37 PULSUS PARADOXUSES :-

(N) $\text{SBP}_{\text{exp}} \& \text{SBP}_{\text{insp}} = 0 \text{ to } 10 \text{ mm Hg.}$

If this difference is $> +10 \Rightarrow \text{Pulsus Paradoxus.}$

Exaggeration of Normal Phenomenon. hence paradoxical word is wrong.

Mech \downarrow in SBP_{insp} more than physio limits.

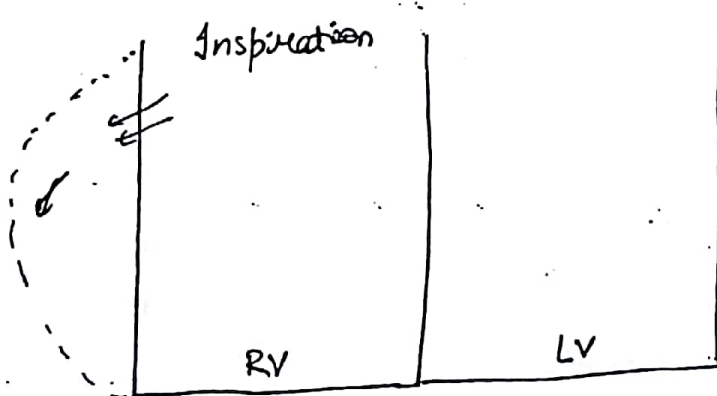
CAUSES

(I) CVS :- H/c CVS cause \Rightarrow Cardiac Tamponade.

"Compression" of heart due to pericardial effusion.

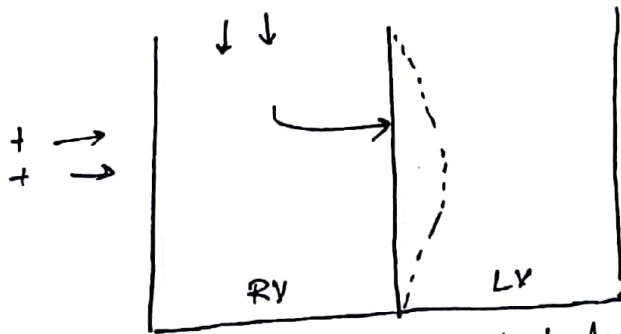
(N) During Inspiration,
Blood flow is more in (R) ventricle.

\downarrow
RV wall dilates to accommodate extra blood.



In Tamponade.
Inspiration
blood.

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RV wall can't dilate due to ~~pleuro~~ pericardial fluid.

→ septal bulge in LV

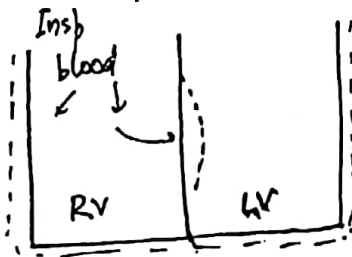
→ ↓ LV filling further

CO ↓

↓ SBP ↓ during inspiration.
than physiological limits.

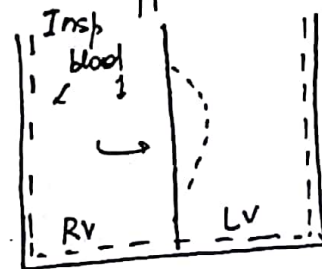
2) Constrictive Pericarditis

Failure of relaxation of heart due to stiff pericardium



3) Restrictive Cardiomyopathy

Failure of relaxation of heart due to stiff endomyocardium.



Septum should be spared from stiffness to cause this ~~side~~ sign

II) Non CVs Cause

H/c overall cause →

Acute Exacerbation of Asthma or COPD.

2) Pulmonary embolism

3) Kussmaul breathing [due to met. acidosis]

4) Obesity

Q. 5) SVC Obstruction [reason not known].

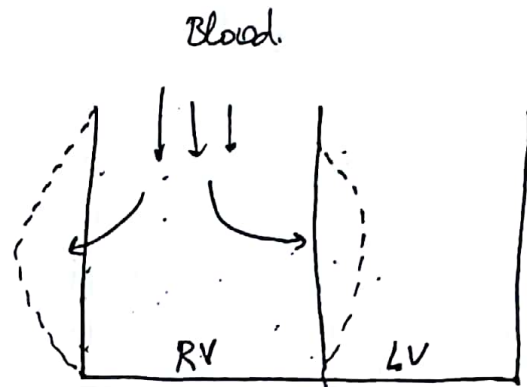
Deep Inspiratory efforts.

↓ Large -ve intrathoracic pressure

↑↑↑ venous return to the right side

↓ Septal bulge.

↓ Pulsus Paradoxus



Due to extra blood septal bulge occurs.

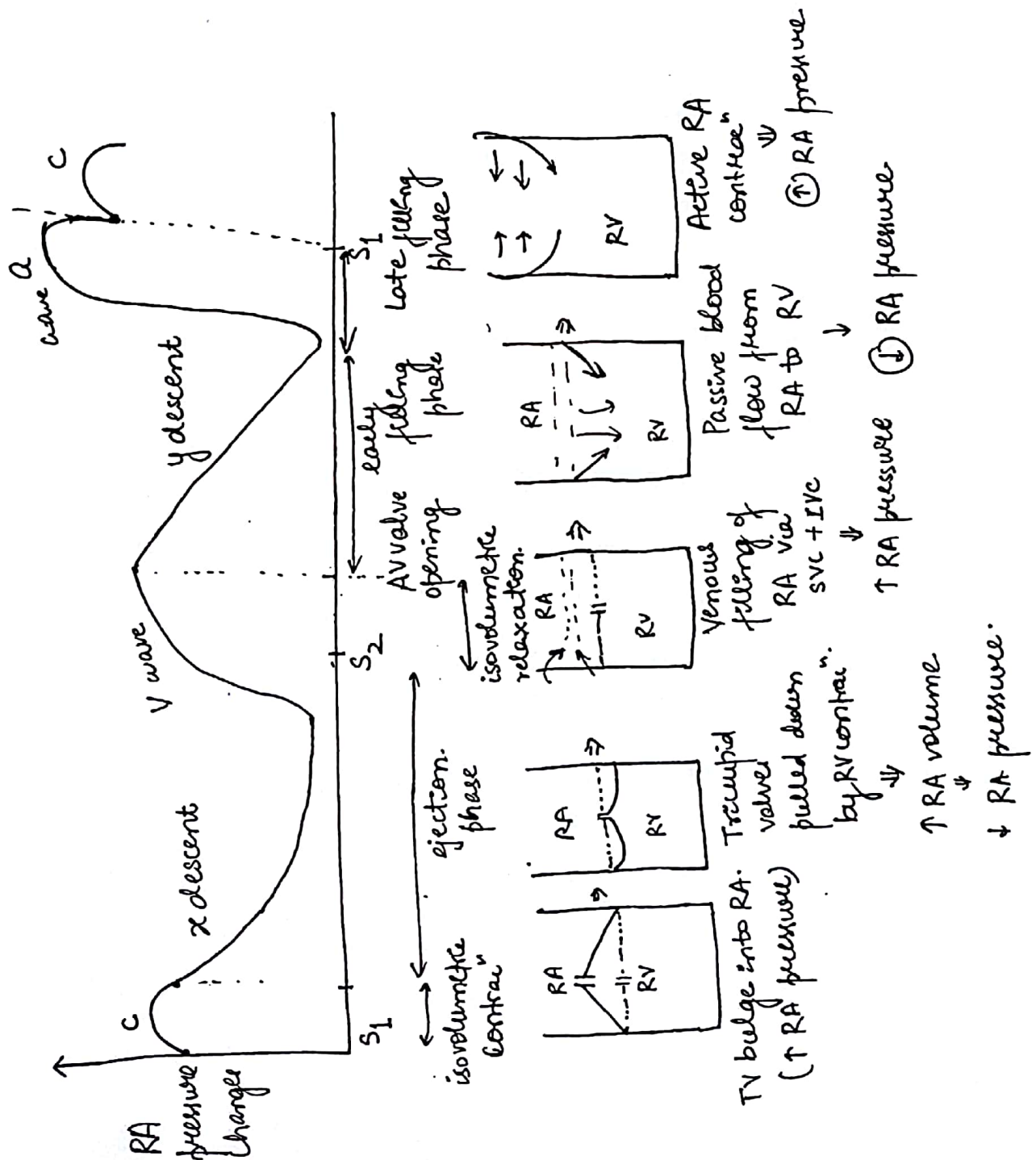
JVP

① - measure of ② atrial pressure seen in ③ IJV

④ Height → 0-3cm from sternal angle

↓ 5cm below
RA activity.

= 5-8cm from RV activity.



Q. ϵ wave is (B) syst + diastolic

\Rightarrow V wave

Q. ϵ wave will be more prominent?

\Rightarrow a wave.

Q. ϵ descent will be more prominent?

\Rightarrow x descent

(I) a wave = due to (R) atrial contraction

1) Absent a wave = if ineffective atrial contraction

↓
AF

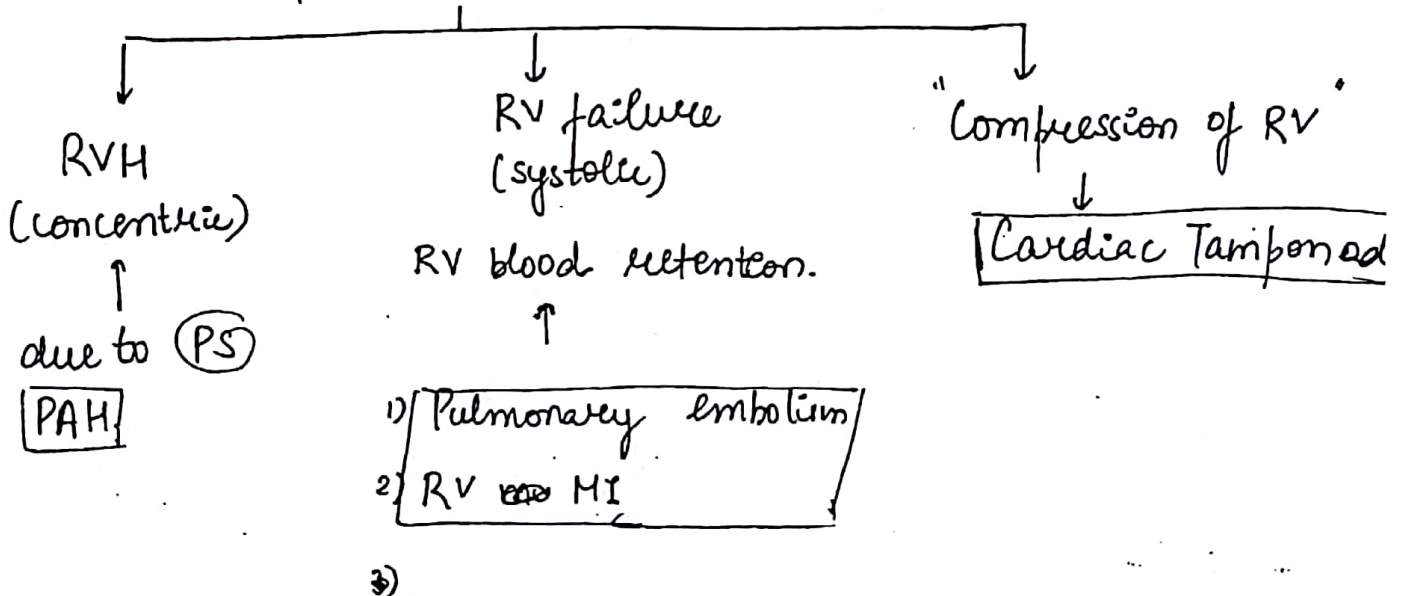
2) Large a wave = if (R) atria contracting against more resistance
Diastolic Wave

If (R) atria is contracting → 1) Tricuspid valve gives resistance
2) RV also gives resistance

cause-

a) Tricuspid stenosis

b) RV pressure ↑



3) **Canon a wave** = if RA contracting against closed T. valve.
(Systolic event) cause TV closure
occurs if RA & RV are contracting simultaneously

Causes → ① **Functional rhythm.**

SA node arrest → AV node becomes pacemaker & impulse reach.
② atria & ventricle simultaneously

Rate of Cannon a wave = 50/min, **regular**

② **Complete AV Block**

SA node will depolarise atria. +
Purkinje fibres will depolarise ventricle
independently.
So occasionally atria & ventricle can depolarise
simultaneously

Canon a wave is = **intermittent**

II **X Descent**

① due to tricuspid ring pulled down by RV
contract. during ejec. phase.

+
② atria is free of significant blood (during this phase)
Ab ①

1) Absent X Descent

if ② atrial pressure doesn't fall as it contains

significant Blood or Clot

Significant blood
↑
(TR)

Clot
↑
(AF)

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② Deep X Descent
occure if tricuspid ring pulled more
downward due to
↑
Increased RV contract

(?)
1) Cardiac tamponade
2) Constrictive Pericarditis.

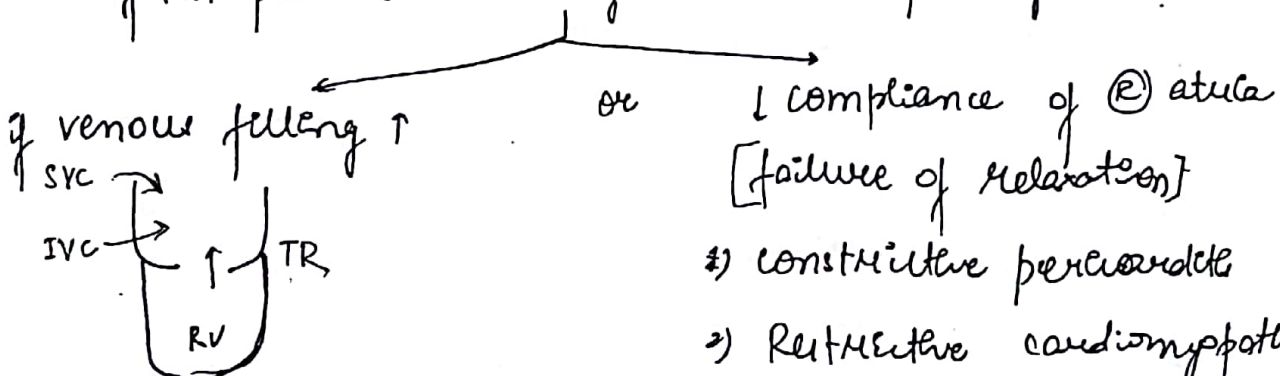
III V Wave

(N) due to venous filling of R atria
Ab(N)

1) Absent or Low V wave :-
occure if venous filling of RA ↓
cause - a) obstructed svc

2) Large V wave :-

If RA pressure ↑ during venous filling



IV Y Descent

(N) due to passive blood flow from (R) atria to (R) ventricle ab(N)

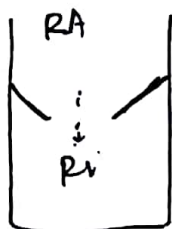
1) Rapid Y Descent :- / FREIDRICH'S SIGN.
will occur if (R) atrial blood moves very fast into (R) ventricle as soon as Tricuspid valve opens.

All causes of large V = Rapidly

2) Slow y Descent :-

If (R) atrial blood moves into (R) ventricle slowly.

cause - 1) Tricuspid stenosis
2) ↑ RV pressure



Causes of Large a = Slow y

y descent absent - if RA blood doesn't move into RV during passive filling phase

↑
occurs if (R) ventricle is fully "compressed".

⇓
Cardiac Tamponade.

Signs of JVP

Description

Causes

① Abdomino Jugular reflex
[abdomen compressed for 10 sec]

if JVP remain elevated by more than 3cm even after release of compression for >15 sec

Latent RVF.
no RVF in basal state
+ RVF is manifested if RV workload ↑

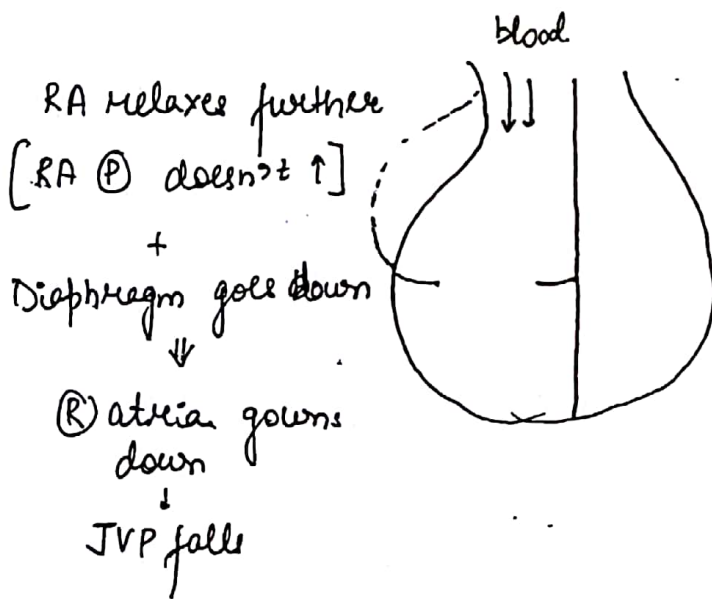
② Kussmaul's sign

↑ in JVP during inspiratory phase

(N) JVP ↓ during inspiration

if (R) atria fails to relax (N)

Constrictive pericarditis
Restrictive cardiomyopathy



If basal RA P if = TS RVF

Basal atrial 'P' ↑ due to

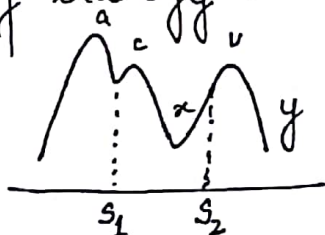
if AV valve Stenosis ... ventricle failure

Kussmaul's Sign is absent in tamponade.

??

Q. Δ of etiology :-

(N)



Ab(N)

①



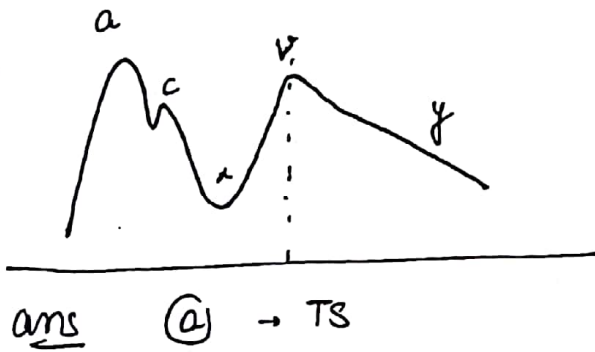
y is absent

a) TS

b) constitutive Pericarditis

c) Tamponade d) TR.

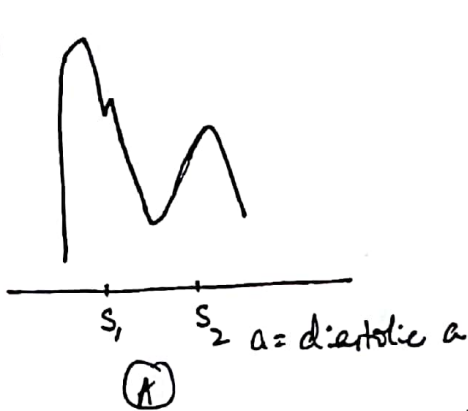
②



Δ = slow y descent

ans (a) → TS

③



(K)

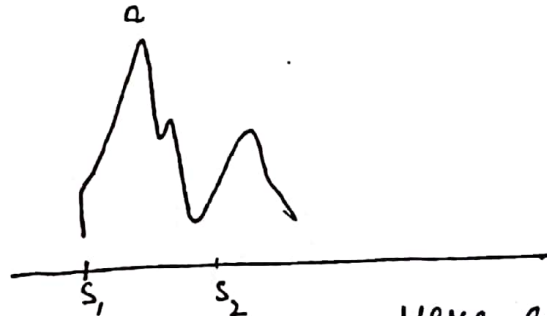
a = diastolic a

Δ = large a TS

Options

① TS

② Junctional Rhythm



(B)

Here a is systolic

Δ = canon A wave

↓
Junctional Rhythm

APEX BEAT

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① due to isovolumetric ② ventricular contracⁿ.

↓

LV apex displaced superiorly

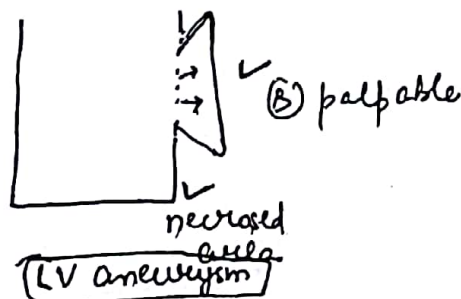
Nature → Tapping.

Site → ① 5th ICS; just medial to mid-clavicular line

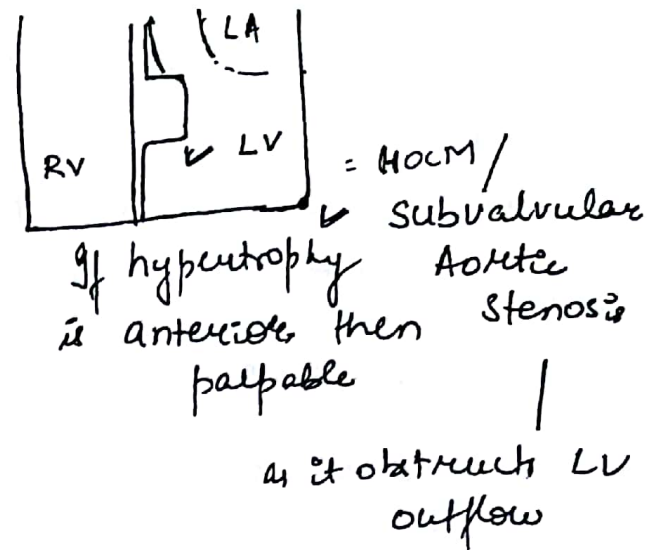
Area → $< 2.5 \text{ cm}^2$ [localised].

Ab ① of Apex

Ab ①	Description	Cause
① Hyperdynamic	Palpable for upto $\frac{2}{3}$ rd of systole	① ventricular volume overload. [↑ CO state]
② Sustained	Palpable for $> \frac{2}{3}$ rd of systole	① ventricle pressure overload. eg. AS.
③ Diffuse	area $> 2.5 \text{ cm}^2$	Dilated cardiomyopathy
④ Double	2 impulses palpable in systole	LV aneurysm (complication of MI)



Asymmetrical septal hypertrophy



⑤ Triple: 3 impulses palpable in systole



⑥ Absent non-palpable

Pericardial effusion

Emphysema

Obesity

Dextrocardia Q

↳ apex goes posteriorly hence not palpable

Q. Double Apex seen in

① As [HOCM & subvalvular As]

② Ts

③ Ms

④ AR.

AUSCULTATORY FINDINGS

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* S_1 .

due to closure of AV valve.

① = M_1T_1 [mainly contributed by mitral valve]

Split < 20 msec.

Site : Apex

* Pitch : moderate

Any mitral valve sound/
murmur.

Best area = Apex

Ab ①

Factors affecting
the intensity

1) Force of isovolumetric
ventricle contraction

Soft S_1

if weak force
↑

eg. Dilated CMP
LVF,
RVF
VSD
§

Loud S_1

Strong force

eg. MS, TS

(if atrial P is high)

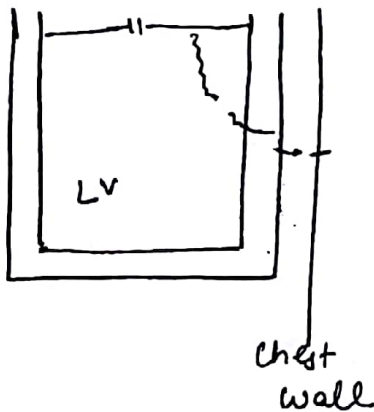
2) Condⁿ of A-v leaflets

if fail to strike
each other

eg. MR
TR

calcification of
leaflet

3) The presence
of fluid,
m/s
air
fat
between AV leaflet
& stethoscope



• if ventricle blood
vol. ↑

AR

PR

• if ventricle wall
thickness ↑

LVH ← AS

RVH ← PS

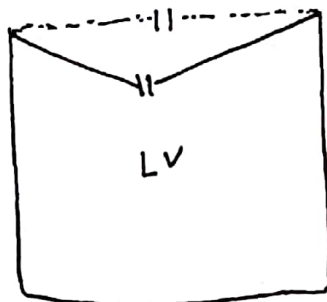
thin. 31
lean.

LMR

All valvular Lesions cause
Soft S, except MS & TS

4) Most imp
factor

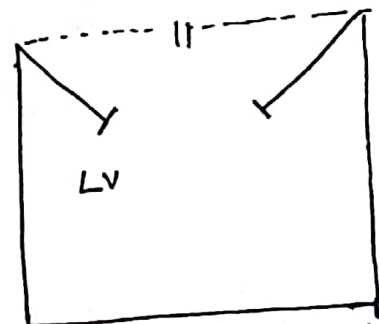
Position of AV
leaflets at onset
of ventricular
contracⁿ.



If impulse reaches ventricle
+ ventricular blood filling fully
complete

↓
AV leaflets pushed to close
position.

- Bradycardia
- PR interval ↑



If impulse reaches ventricle
fast +
ventricle blood
filling incomplete

↓
AV leaflets fully
open.

Tachycardia
short PR interval

Q. In Hypothyroidism, S_1 is soft.

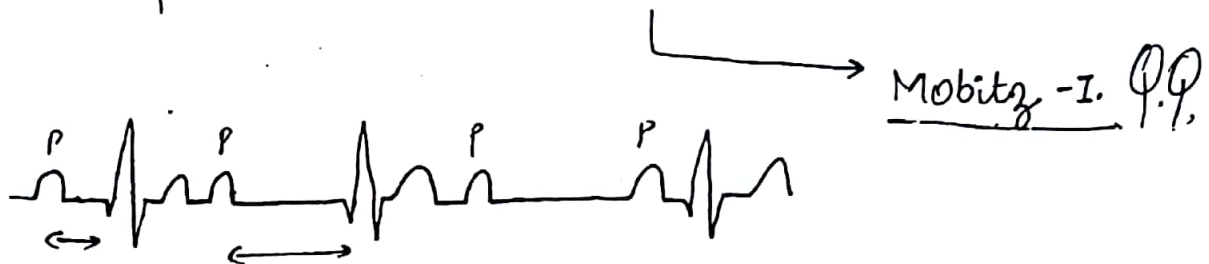
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Q. In Digoxin effect, S_1 is soft and AV Block \rightarrow PR \uparrow interval

Q Condⁿ causing variable S_1 intensity :-

If variable HR = AF

Q If variable PR interval = 2° AV Block



Progressively PR interval \uparrow till atrial impulse fails to conduct to ventricle
= Wenkebach's phenomenon.

* S_2

It is due to closure of Semilunar Valves.

(N) - $A_2 P_2$

Aortic valve closes earlier than Pulmonary valve
 \downarrow

LV ejection time is less than RV

Site = For A_2

aortic area

(R) 2nd ICS

For P_2

Pulmonary area

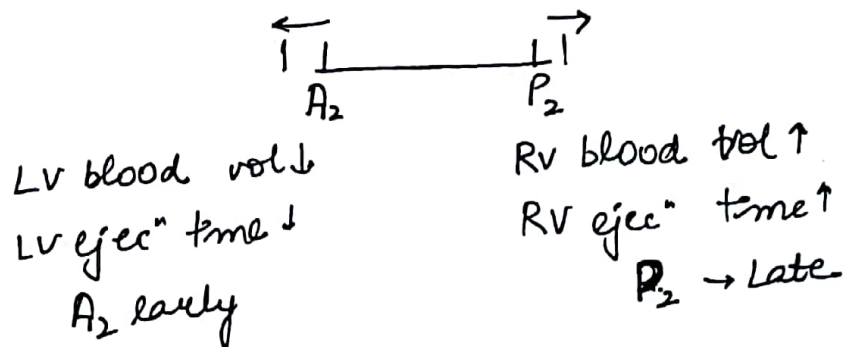
(L) 2nd ICS

Best for S_2 \rightarrow Pulmonary area. [as both sound heard]

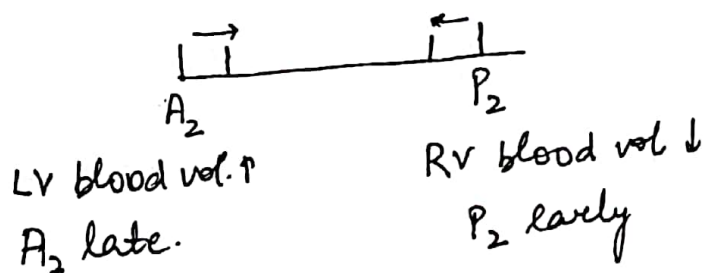
Split = 30-60 msec.

During Inspiration → split Increase

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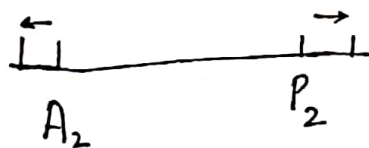


During Expiration → split Decreases or Expired



Ab (N) of S₂ split

① Wide split



CAUSES

1) Early A₂. (earlier than physio limit)

↓ If LV ejection time ↓

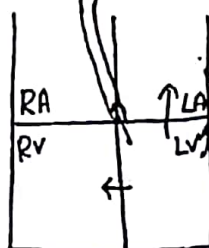
VSD
MR

or

↓ If LV early depolarisation.

WPW syndrome

Misc → (L) Q.



accessory pathway.

from LA to LV
will depolarise
LV early.

Q (Bundle of Kent)

→ Type A WPW syndrome

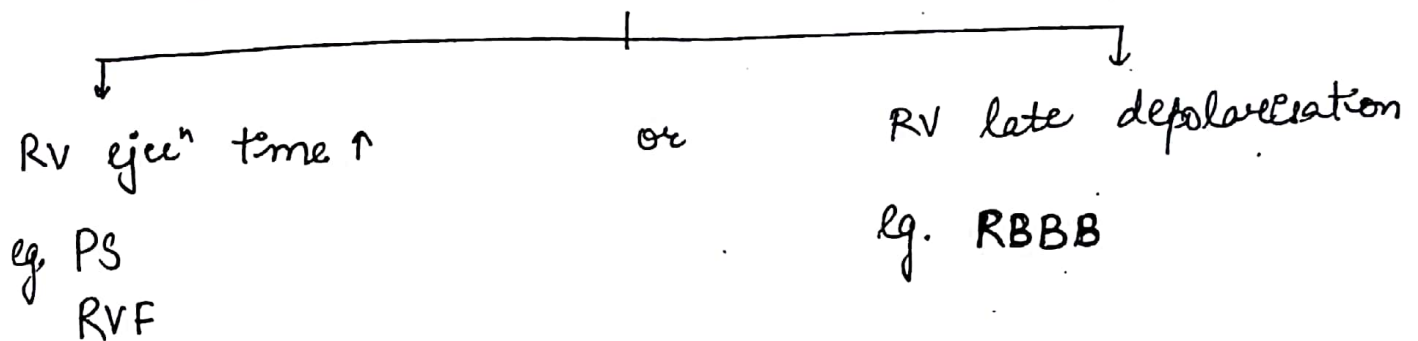
1) $\sigma > \phi$

2) (L) side more common

3) short PR interval

4) S₁ will be soft Q. ... ?

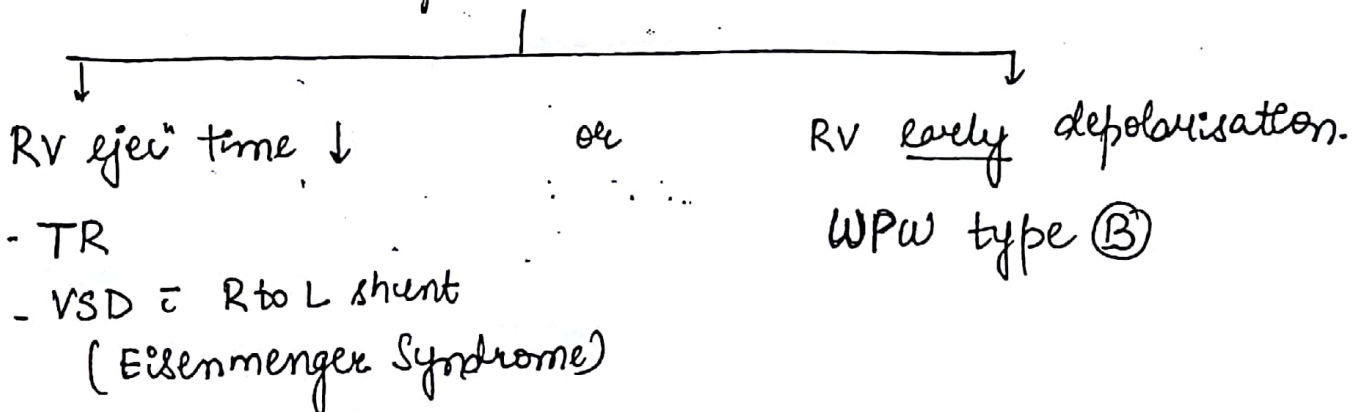
II) P₂ is Late [Later than physio limit]



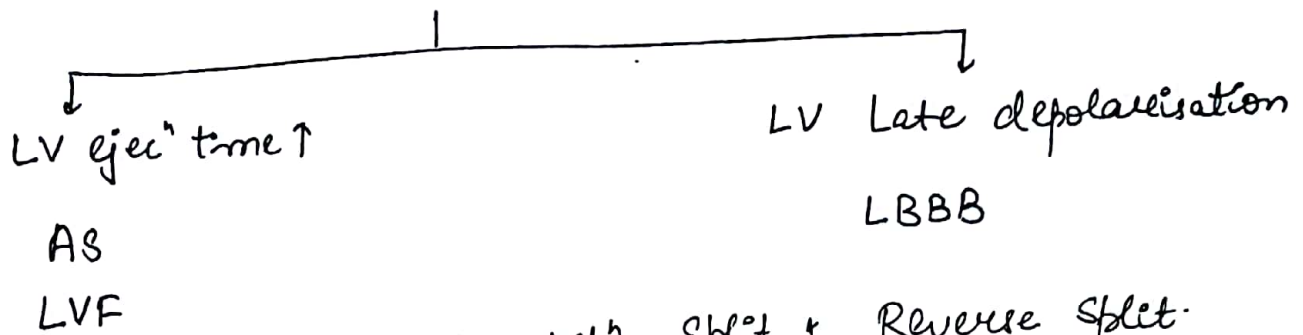
② REVERSE SPLIT or PARADOXICAL SPLIT
CAUSES

P₂ A₂

① P₂ is early (earlier than A₂)



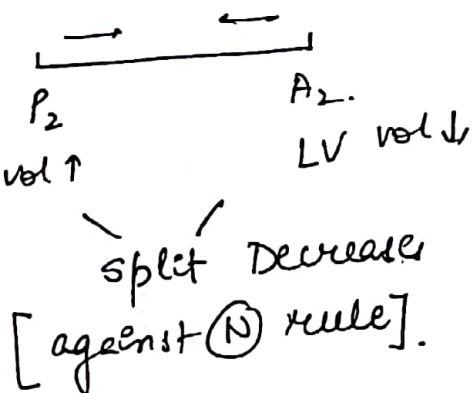
② A_2 is Late (later than P_2)



Q. How to differentiate betⁿ Split + Reverse Split.

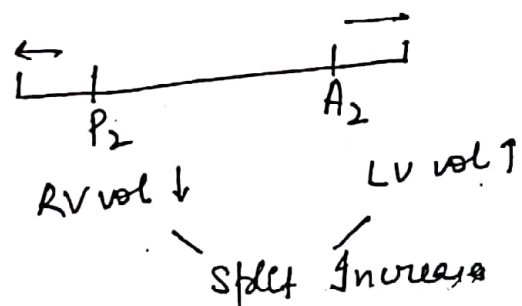
During Inspiration.

Reverse split will Decrease RV vol ↑



During Expiration

Reverse split will Increase



Q. In. Pulmonary artery HTN, S_2 split

Ⓐ ↓

Ⓑ ↑

Ⓒ No change

→ P_2 comes early ----?

Hint - Pulmonary hang out interval

③ WIDE + FIXED SPLIT

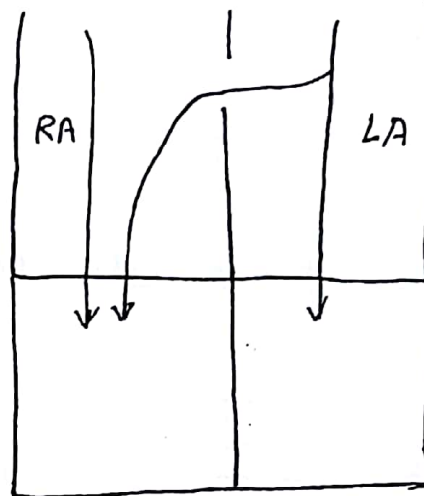
36

doesn't vary w/ resp. phases.

cause → ASD.

RV blood ↑ → P_2 late
 LV blood ↓ → A_2 early

wide



Split is fixed
 = ventricle blood vol
 remain constant
 during Insp. & Exp.

↓

RV blood → Insp. = $\uparrow + \downarrow$
 Exp. = $\downarrow + \uparrow$ ⇒ Fixed.

Intensity of S_2

Factors

1) Pressure of aorta/
 Pulmonary to close
 SL valves.

Soft

Hypotension

Loud

Systemic HTN
 → A_2

P. HTN → P_2

2) Condⁿ of SL valves
 Leaflets.

calcified

AR
 PR

x

* Single S_2 seen in

AR [A_2 is absent]

PR [P_2 absent]

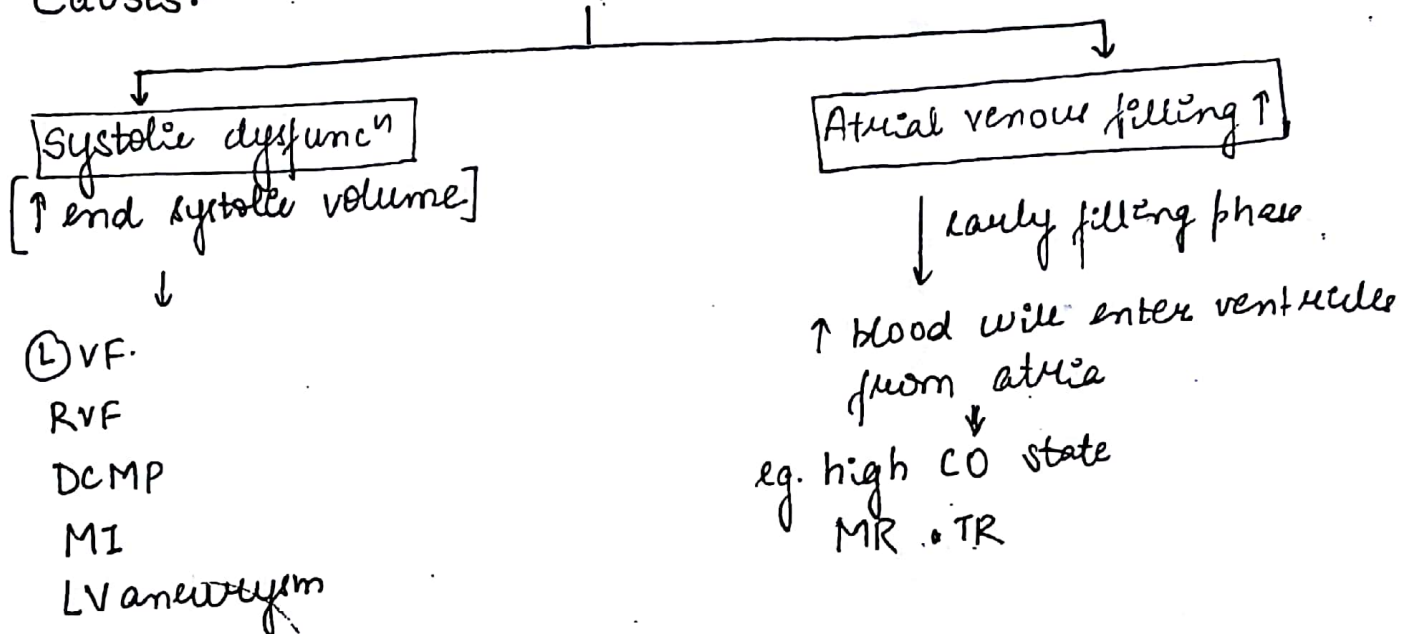
AS/PS [valves get severely calcified]

S₃ / Ventricle Gallop

It is due to ↑ in ventricle blood volume during early filling phase.

ventricle vibrations

Causes:-



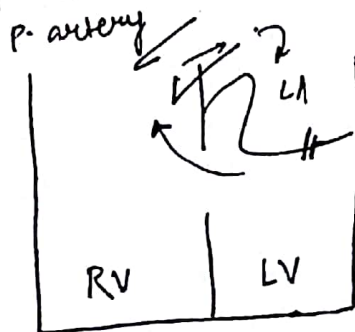
Site → LV S₃ → Apex

RV S₃ → Tricuspid area. [(L) lower parasternal]

Pitch → Low pitch.

Q. In atrial septal defect = side S₃ → RV S₃ / LV S₃ ?
Ans → RV S₃.

Q. In VSD, = side S₃ = LV S₃



Pulmonary valve is open in systole
So blood from VSD goes into

P. artery ↓

P. vein ↓

(L) Atrium

MV is closed in systole & blood is collected in it 38
1st chamber to enlarge is (L) atria.

Q. In PDA $S_3 = LVS_3$

S_4 / Atrial Gallop

It is due to atria contracting against stiff ventricles \rightarrow ventricle vibrate

Causes -

- 1) Restrictive CMP
- 2) HOCM
- 3) LVH due to AS
- 4) RVH due to PS
- 5) Acute MI.

In acute MI Both S_3 & S_4 .

\downarrow Relaxation

\uparrow

\downarrow ATP due to ischaemia.

Site - $LVS_4 \rightarrow$ Apex

$RVS_4 \rightarrow$ Tricuspid area

Pitch - Low pitch.

Q. S_3 can be physiological (True) / False

Ans \rightarrow \oplus • young children & athletes

Q. S_4 can be physio - True (False)

Q. S_3 represents systolic failure

Q. S_4 represents Diastolic failure

Q. S_4 seen in all except

a) AS [LVH]

b) Constrictive Pericarditis [ventricles are trapped \rightarrow can't vibrate]

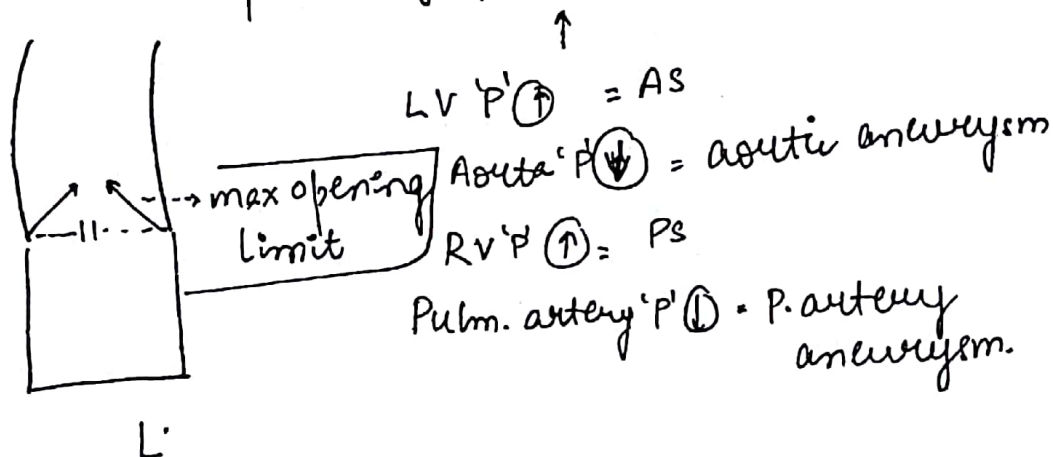
c) AR \rightarrow extreme LV dilatation \rightarrow making it stiff

d) Amyloidosis [RCMP]

Constrictive Pericarditis doesn't produce S_3 + S_4 .

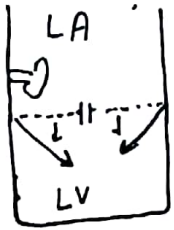
ADDITIONAL HEART SOUNDS

Name	Cause	Timing	Pitch
Ejection click	due to sudden cessation of opening of SL valves as it opens $\bar{=}$ high pressure	S_1 S_2 early systole	High.

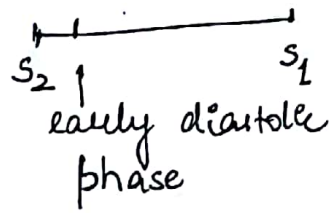


Ejection click ↓ in calcified lesions.

2. Opening Snap

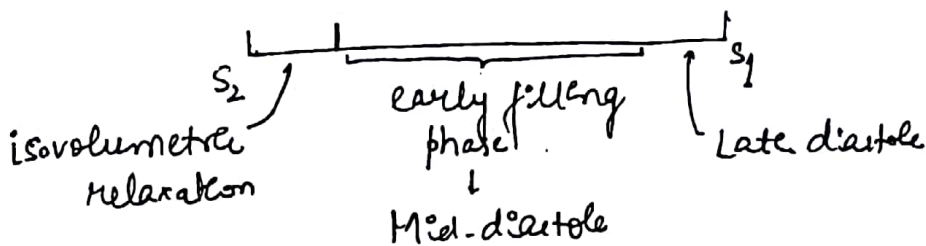


sudden cessation
of opening of AV
valve as it
opens to high pressure



High

LA pressure ↑ = MS, LA myxoma
RA pressure ↑ = TS



③ Tumour Polyp

④ Atrial myxoma
striking mitral valve

Early diastole

Low

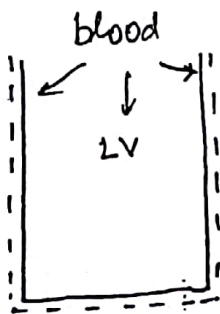
QQ

④ Pericardial Knock

ventricle wall
strike [knock] on
stiff pericardium

Early filling
phase

High



Most specific sign
of

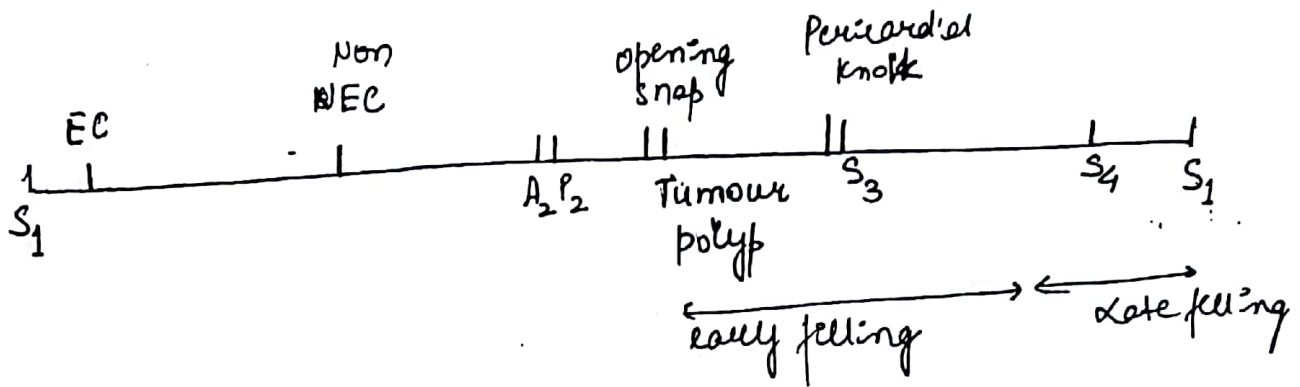
Constrictive
Pericarditis

⑤ Non-ejection Click

MVP prolapse

mid
systole

High

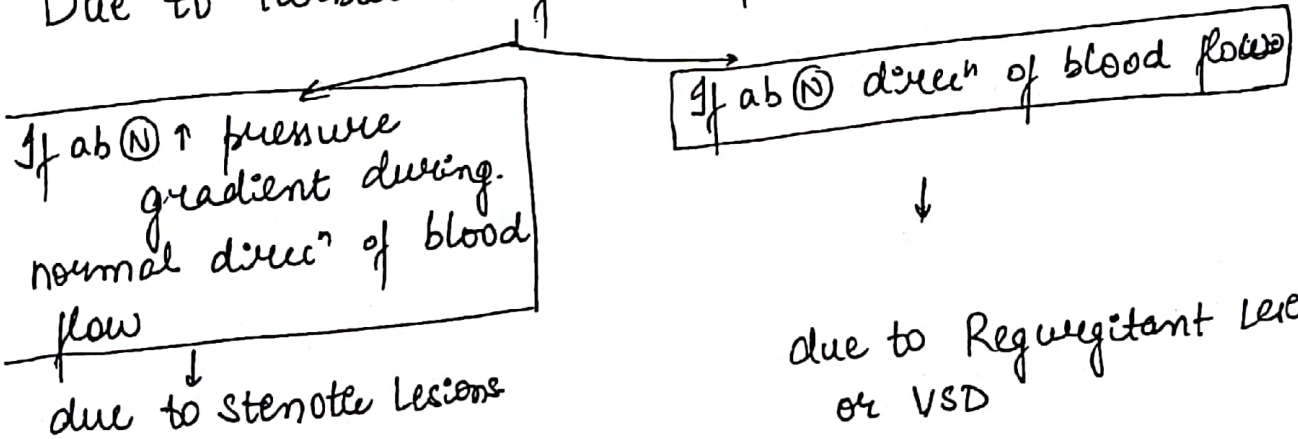


In AF. JVP = a wave absent

HS = S₄ ⊖ [if previously present]

MURMURS

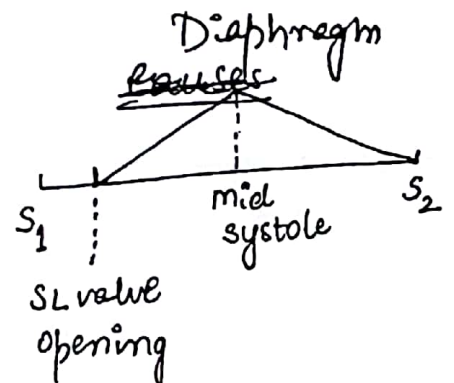
Due to turbulence of blood flow in the



TYPES

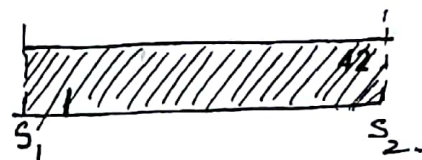
(I) SYSTOLIC MURMURS

Name	M/c murmur overall	Cause
① Ejection systolic murmur	or	due to turbulence of blood flow due to ejection phase
Mid-systolic murmur	or	AS, PS
Crescendo-Decrescendo	or	↑ CO states. → [⊙]
		(↑ blood flow across SL valves)



② Pansystolic
Murmur
No peak.

VSD
[LV pressure remain $>$ RVP
throughout systole]



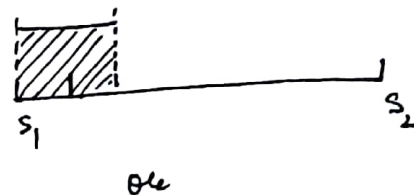
chr MR

[LV 'P' remain $>$ LA 'P'
throughout systole]

Chr. TR.

Q Q.
③ Early systolic
murmur

If defect closes before
mid-systole
eg. ② Small muscular VSD



If pressure gradient becomes
zero (\leq mid-systole)



⑥ Acute MR. \rightarrow
[MI or IE]. LA is not dilated unlike
chr. MR.

During early systole, ① ventricle blood enters LA

LA 'P' will \uparrow rapidly

during mid systole ② atrial 'P' = ① ventricle 'P'
murmur will stop

④ Late systolic
murmur

③ Acute TR:
MV Prolapse



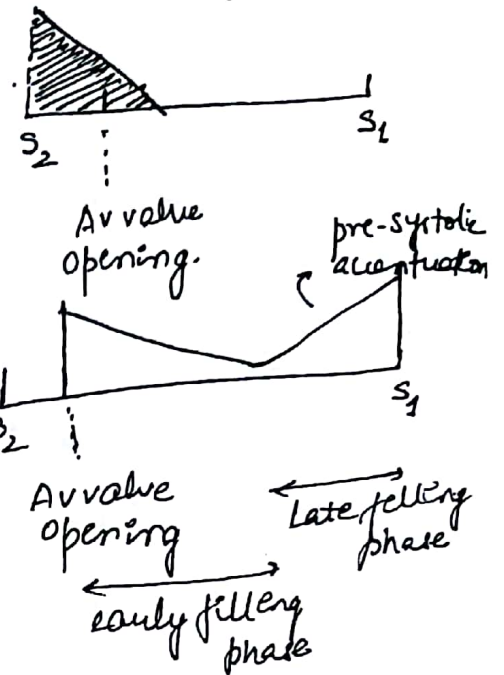
(II) DIASTOLIC MURMURS

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Diagram

Name Causes

1) Early Diastolic murmur.
or
Decrescendo Murmur AR, PR



2) Mid-Diastolic murmur Turbulence of blood flow from atria to ventricles
MS, TS

Q. Early Systolic murmur seen in all except
a) TR (acute)
b) VSD (small muscular)
c) papillary m/s necrosis (MI → acute HR)
✓ AS

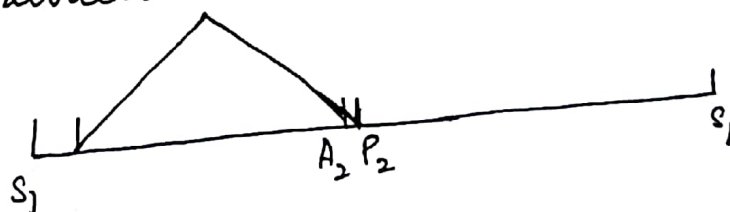
Q. Identify the valvular lesion

(a) MS

(b) TS

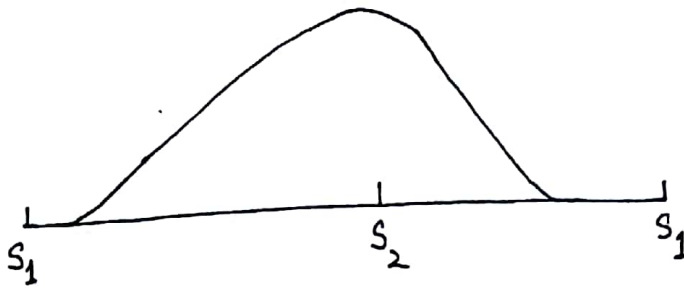
(c) PS

(d) AS



III CONTINUOUS MURMUR

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- Starts in systole
 - Peaks around S_2
 - Ends in Diastole
- Origin - single site

Mechanisms:-

If Ab @ pressure gradient is maintained throughout
Systole & Diastole

If Defect remains open throughout Systole & Diastole

Continuous murmurs are never due
to valvular lesions

CAUSES:-

1) Ab @ communication b/w artery to vein

eg. A-V fistula

Ruptured sinus of valsalva
(acute to chronic connection)

2) Ab @ communication b/w systemic to Pulm.

eg. PDA

③ ↑ blood flow into blood vessels
 mammary artery souffle (lactation)
 uterine artery souffle (♀)

45

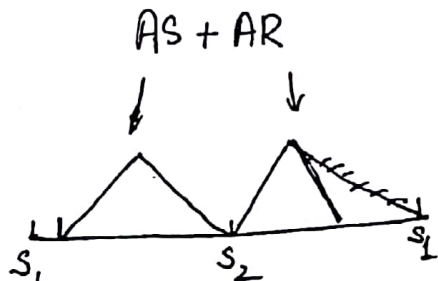
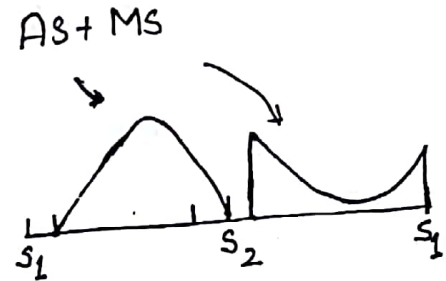
④ Severe arterial stenosis [70% narrowing of diameter]
 Renal artery stenosis → 'bruit'

Q. Continuous murmur can be physiological True/false
 4 ♂, Lactation

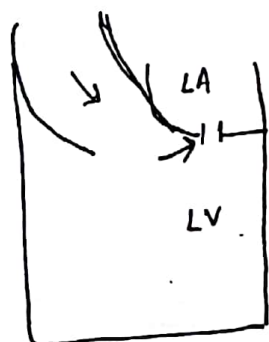
Q. All causes continuous murmur except:

- a) Pt. of CKD on haemodialysis [A-v fistula]
- b) severe atherosclerosis [carotid or renal artery stenosis]
- c) AR + AS
- d) Lactation.

D/D of Continuous Murmur.

	<u>Continuous murmur</u>	<u>TO & FRO</u>	<u>Systolic-diastolic</u>
	✓	✓	✓
Systole + Diastole			
Origin	single site	single site	Different sites
Peak around S ₂	✓	X	X
eg.	✓		

<u>Name</u>	<u>Cause</u>	<u>Type</u>	<u>Site</u> 46
1) Gibson's murmur	PDA	continuous	① upper parasternal area
2) Key Hodgkin's murmur	AR	early diastolic	① 3 rd ICS = Erb's area = Neo-aortic area
3) Graham-Steel's murmur	PR	early diastolic	① 2 nd ICS Pulmonary area
4) Austin flint murmur	AR Regurgitant jet of AR striking mitral valve.	mid-diastolic to late	Apex
5) Carey Coomb's murmur	ARF Turbulence of blood flow over inflamed rough mitral valve	mid-diastolic murmur.	Apex
6) Dock's murmur	Severe stenosis of LAD artery (widow's artery)	continuous murmur.	3 rd ① ICS 4cm from sternal margin



⑦ Still's murmur

young children

Ejection systolic murmur

Pulmonary area

= Innocent murmur

(relatively ↑ blood flow across Pulm. valve)

⑧ Rydand's murmur

complete Av Block.

mid-diastolic

apex.

↓
↑ Blood flow across Av valve

FACTORS AFFECTING MURMURS:-

If blood flow ↑ → all murmur will ↑ except

↓ MVP

HOCM.

Murmur

Blood flow

1) Respiratory variation.

a) Inspiration

↑ blood on (R) side

↑ TS, TR, PS, PR
exception

Pulmonary ejection click
↓ in inspiration

b) Expiration

↑ blood on (L) side

↑ MS, MR, AS, AR

[except HOCM, MVP]

c) Valsalva effect

(Persistent expiration)

Persistent expiratory
↓ blood on (R) side
followed by (L) side.

All murmur will ↓
[except HOCM, MVP].

II Postural Variation :-

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a) Standing

↓ blood flow into R+L side

all murmurs will ↓
except HOCM, MVP

b) Squatting
(immediate effect)

↑ blood flow into R+L side

all murmurs will ↑
except HOCM, MVP

III Effects of Afterload changes :-

Lesion

Afterload ↓
(aorta 'P' ↓)

Afterload ↑
(aorta 'P' ↑)

AS

murmur ↑

murmur ↓

Pressure gradient

$$= \text{LV 'P'} - \text{aorta 'P'}$$

AR

murmur ↓

murmur ↑

Pressure gradient

$$= \text{aorta 'P'} - \text{LV 'P'}$$

MR



murmur ↓



murmur ↑

Regurgitant lesions behave similar

MVP

49

Cause - Deficiency of type III collagen in MV leaflets (posterior)

↓
↑ leaflet flexibility
↓
surface area of MV leaflet ↑
↓
too big for LV cavity

C/F

Symptoms:-

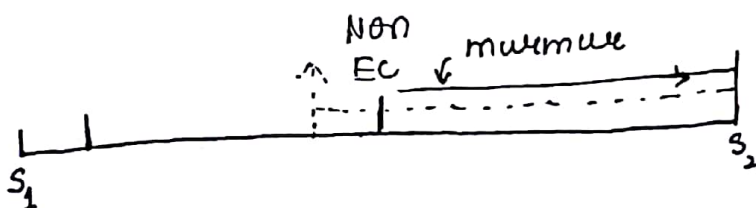
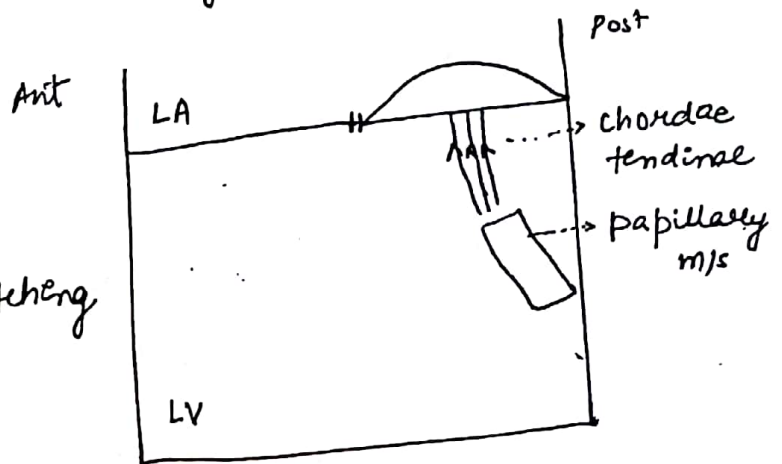
1) chest pain
M/c symptom.
Due to papillary m/c stretching

2) Palpitations
ventricle fibre stretching
↓
produce ventricle ectopic

Sign:-

▷ M/c sign → Non-lyceⁿ click.
due to doming of MV
It occurs when LV cavity size ↓ significantly

2) Late systolic murmur (MR)
occure when post. leaflet looses contract = ant. leaflet



If LV cavity blood vol. ↓ → Prolapse will occur early
[standing position]
[inspiratory phase] ↓
Non-Ejecⁿ Click earlier.
↓
murmur will start earlier

Inv

D2D Echo
if prolapse is > 2mm into LA

T/t

- 1) Reassurance. (mostly benign)
- 2) β blockers (if palpitations) DOC
- 3) S_x repair ← NYHA symp $\geq II$
+
Severe MR on Echo.

HOCM

51

Cause - AD

mutation of β -myosin heavy chain.

["Private mutations"]



Asymmetrical proliferation of septum.
near the LV outflow tract.



Free wall hypertrophy



Diastolic funcⁿ
↓ as filling
is impaired



LV systolic function ↑
to overcome obstruction

C/F

Symptom :-

1) Earliest → Dyspnoea ← $LA^P \uparrow \leftarrow LV^P \uparrow$

2) Angina ← ↑ LV workload.

+
Coronary vessels compressed by hypertrophied
myocytes.

3) Syncope



Fixed CO [CO will not ↑ during
demand]

4) * Sudden cardiac death

→ Irreversible loss of
cardiac funcⁿ

̄ in 1 hour of symptoms

→ HOCM is H/cc.

→ SCD is due to ventricular arrhythmias due to ischaemia
⑤ ↓
⑥ Na^+/K^+ ATPase.

Signs:-

1) Pulse = Bifid
or
Pointed finger pulse

2) JVP :

If hypertrophied septum bulge into (R) atrium

Bernheim's effect Systolic funcⁿ

↓
RV 'P' T
↓

- A⁺
- y slow

3) Apex = Double / Triple

4) S₁ = Intensity soft

S₂ = Split Reverse

S₃ = rare

S₄ = LV S₄ ++

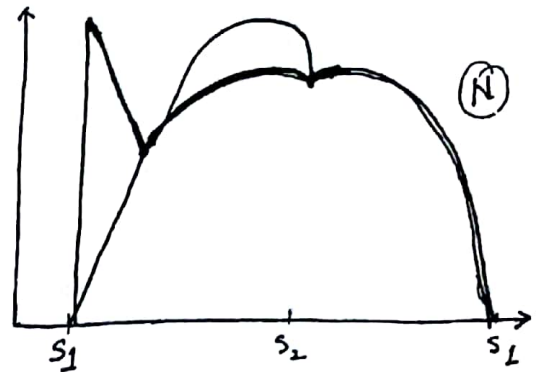
QQ

5) Most characteristic sign:-

Type → Ejection systolic

Site → (L) 3rd ICS Erb's area

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Brick grove. → Percussion wave will be early
contractⁿ

Tidal wave low
due to obstructⁿ of
blood flow

↑ A₂ late
LV ejection time ↑
(due to obstructⁿ)



(SAM)
systolic ant. movement of mitral
valve toward septum
further ↑ing the obstruction.

2 most imp factors
affecting obstruction

① Contractility

if ↑ → SAM ↑ → obstruction ↑

② Blood in LV if ↓ → obstruction ↑
(preload)

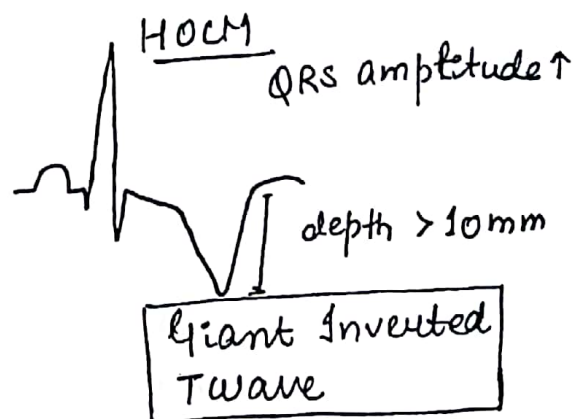
(Blood act as physical barrier separating
MV & septum)

Intd

1) CXR → cardiac size (N)

2) ECG →

→ (N)



3) Echo - $\frac{\text{septum thickness}}{\text{LV free wall thickness}}$

$\frac{3}{1}$ [reversed from (N)]

Drug

Digoxin. C/I in HOCM.

Diuretics

Veno Dilators

Rx

54

1) β blocker \rightarrow Initial DOC

If CI \rightarrow Non DHP CCB.

Doesn't prevent sudden cardiac death.

2) AMIODARONE

given if post MIO ventricular arrhythmia

3) Implantable defibrillator. Device (intracardiac)
 \hookrightarrow prevent SCD

4) Septal artery sclerosis [ethanol]
 \downarrow
causes regression of septum.

LMP

ARF

12/2/18

55

Cause:-

Hypersensitivity reacⁿ to Group A β haemolytic
Streptococci [Pharyngitis]
Type II HSN Reacⁿ.

C/F & Inv:-

Modified Jones Criteria

Major:- (5)

① Arthritis

Unique features

M/c major ~~manifestation~~

Large joints

asymmetrical

migratory

Non-erosive (non-deformity)

Polyarthritis

Exception - JACOUD's
arthropathy
(deformities +)

Duration ≤ 4 wks

Rx

DOC - Aspirin

75mg / 19/day

② Carditis

M/c Valvular
Lesion in
RHD = MS

M/c C of Death = CHF

M/c layer = Endocarditis

M/c valve = Mitral

M/c Lesion = MR

L/c Valve = Pulmonary

Myocarditis = no necrosis
[Troponin - (N)]

Pericarditis \rightarrow Tamponade
Constrictive
Pericarditis } very rare

DOC Diuretic
 \downarrow no response
Steroid
 \downarrow no response
Valve
replacement

③ Sydenham's Chorea

[Ab against basal ganglia, cerebral cortex]

Motor = Tongue
fibrillation
+

Ext. Rotation of hand
["scooping"]
+

"Milking action"
Disappear in sleep

♀ > ♂
+

Late manifestation
> 1-7 months

Neuropsychiatric
disorders

Sedation

↓ no response
valproate.

↓ no response

IVIg ♀♀:
(for refractory cases)

④ Subcutaneous Nodules

Site: extensor
surface

Non-tender

Size: 0.5-2 cm

No t/t required

⑤ Erythema Marginatum

Site: extremities
Trunk

(never on face)

Serpentine edge
progress fast

t/t Not required

Minor Manifestation

Clinical

- 1) Fever (M/C Symptom)
- 2) Arthralgias

Lab

- 1) ↑ ESR
- 2) ↑ CRP
- 3) ↑ PR interval on ECG.
- 4) [due to AV node inflammation]

Essential Criteria

- 1) Evidence of recent streptococcal infection
(< 45 days)

n/o scarlet fever
is removed now

Any one of 3 criteria -

a) Throat culture +ve

b) Ab +ve for [ASO ↑ &/or AntidNAse]

c) Rapid Streptococcal Ag test

Minimum criteria needed to make Δ of

Clinical	Major	Minor	Minor Essential
1) 1° ARF	2 major 1	- or 2	1 + +
2) Recurrent ARF		3	+
3) Recurrent ARF on established RHD	-	2	+
4) Sydenham's syndrome chorea	-	-	-
5) E Indolent carditis (\bar{c} out any h/n cause)	-	-	-

Changes in Jones Criteria.

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Low Prevalence
ARF < 2/1 lakh school
going children

High Prevalence
72/1 lakh [India].

Major

Joint Involvement
= Polyarthritides

Polyarthritides
or
Monoarthritides
or
Polyarthralgia

Minor

Fever $> 38.5^{\circ}\text{C}$

$> 38^{\circ}\text{C}$

Arthralgia - Polyarthralgia

Monoarthralgia.

ESR $> 60 \text{ mm/hour}$

$> 30 \text{ mm/hour}$

Prophylaxis:

1) 1^o Prophylaxis:- Streptococcus $\xrightarrow{\text{X}}$ ARF
pharyngitis

➤ Ab of choice = Benzathine Penicillin Single Dose
(1.2 mU) if $> 27 \text{ kg}$

if ~~27~~ 0.6 mU if $< 27 \text{ kg}$.

Should be started less than 10 days of Pharyngitis

↓ if penicillin allergy

Macrolides (Erythromycin or Azithromycin)

27 2° Prophylaxis

ARF \rightarrow Recurrent ARF

59

Ab of choice = Benzathine Penicillin.
(1.2 or 0.6 MU)

every 3-4 wkly

↓ if allergy to penicillin

Sulfadiazine Q

↓ if allergy

Macrolides

Duration of 2° prophylaxis:

Clinical Δ

1) 5 years or till pt's age 21 yrs
[ever is longer]

ARF \bar{c} out
carditis

2) 10 yrs or till pt's age 21 yrs.
[ever is longer]

ARF \bar{c} carditis

3) India - Lifelong ideally
10 years till pt's age 40 yrs
[ever longer]

ARF \bar{c} RHD established

D/D of ARF :-

1) Post-Streptococcal Reactive arthritis (PSRA) :-

- Small joints
- Symmetrical
- Duration > 1 month.
- Poor response to aspirin.

② P - paediatric

A - autoimmune

N - neuropsychiatric

D - Disorder

A - associated i

S - streptoc.

→ NO other ARF manifestations⁶⁰

Complications of ARF.

VALVULAR HEART DISEASE.

MS

Cause- M/c - RHD

M/c non-rheumatic
= congenital

Pathophysiology:

↑ LA 'P' (dyspnoea
early
symptom)

↓
↑ Pulm. Vein
followed by

↑ Pulm. artery 'P'

↓
RV pressure overload.
↓ remodelling

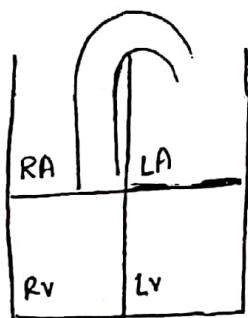
RV [concentric hypertrophy]
↓ Later

RV systolic failure

↓
RV blood retention occur

↓
RA 'P' ↑ ↔ Systemic vein
'P' ↑

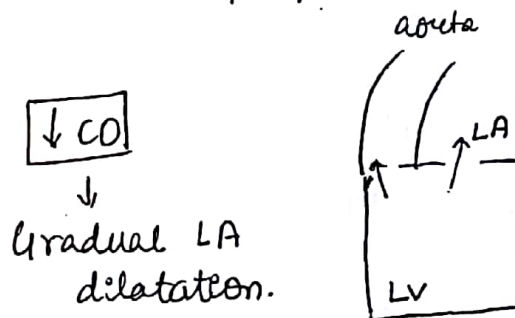
↓
2nd site of stenosis → Pulmonary
artery.



MR

M/c - RHD

M/c non-rheumatic
= MVP



↓ CO
↓
Gradual LA
dilatation.

↓ during diastole
↑ blood will move from
LA to LV

↓
LV volume overload.

↓ Remodelling
LV eccentric hypertrophy.

↓ later
LV systolic failure
↓
LA 'P' ↑

CO ↓

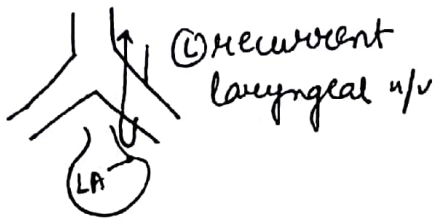
Symptoms Mech

① Dyspnoea \leftarrow LA P' \uparrow

② Haemoptysis \leftarrow M/c source
= Bronchial veins

③ Anasarca \leftarrow systemic veins
hydropic $P' \uparrow$

④



Hoarseness of
voice

[Ortner's syndrome]

Signs

Pulse - irregularly irregular
rhythm

Pulse Defect

Due to AF
Pulse

(+)

(+)

(+)

(+)

due to AF

JVP \rightarrow

Reversal
occur

Absent

Prominent

a

v

x

y

Apex - LV (N)

Site - (N)

Nature - Tapping

Symptoms

① Fatigue

② Palpitations

③ Dyspnoea

Mech

\downarrow CO

\leftarrow LV force of
contraction \uparrow

\leftarrow LA P' \uparrow

LV - Dilated + vol. overload

Site - Shifted laterally

Nature - Hyperdynamic

Auscultatory signs

S_1 = Loud
exception - if calcified valves

S_2 = split - wide

if RVF occur $\rightarrow P_2$ late.

S_3 = never LVS_3

if RVF $\rightarrow RVS_3 +$

S_4 = if RVH $\rightarrow RVS_4$

Opening = +ve
snap

becomes \ominus if calcified valves.

Murmur.

(1°)

Typ = mid-diastolic

Site - Apex

Pitch = Low pitch

if pressure gradient < 40 mmHg
= low pitch murmur

Radiation - Nil

Best pt's position - (L) Lateral Decubitus

Phase - expiratory

62

S_1 = soft

S_2 = split - wide.

LV ejcⁿ time \downarrow = A_2 early

S_3 - LVS_3 ++

S_4 : $LVS_4 \pm$ [in late MR due to
extreme LV
dilatation making it
steff]

Opening = -ve
snap

(1°)

Typ - pan-systolic

Acute MR = early systolic
MVP induced = late systolic

Site - Apex

Pitch - High pitch

Stenotic lesions are low pitch
Regurgitant " are high pitch

Radiation - Interscapular area
Axilla

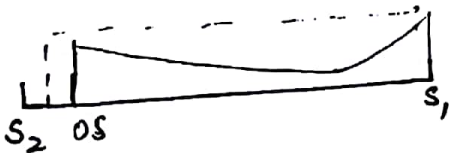
Best pt's position - (L) Lateral decubitus

Phase - expiratory

2° murmur = ⊖

Clinical Criteria for Severity

- 1) Opening snap
S₂-OS gap inversely related to severity



- 2) Length of murmur is directly related to severity

Ix

ECG - Sequence

- ① LAtrial enlargement

↓

- ② RVH signs

↓

- ③ RA enlargement

Biatrial enlargement
= due to MS

CXR

①



→



straightening of
① upper border.
(earliest)

2° murmur

↑ blood flow across MV₆₃ during diastole due to ↑ blood.

= mid-diastolic murmur

= Functional MS → severe MR

- 1) Apex = shifted laterally

- 2) S₂ = wide split

- 3) S₃ = +ve of LV S₃

- 4) murmur = mid-diastolic

Loudness or intensity is never a criteria for severity in Valvular Heart Disease

Ix

ECG

- 1) LAE

↓

- 2) RVH signs LVH signs.

CXR

✓

② Double atrial shadow



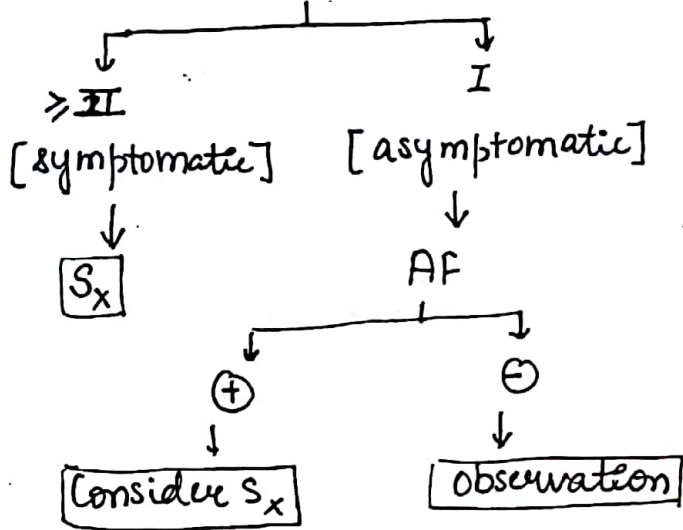
very rare.

64

Rx Severe MS [area $< 1.5 \text{ cm}^2$]

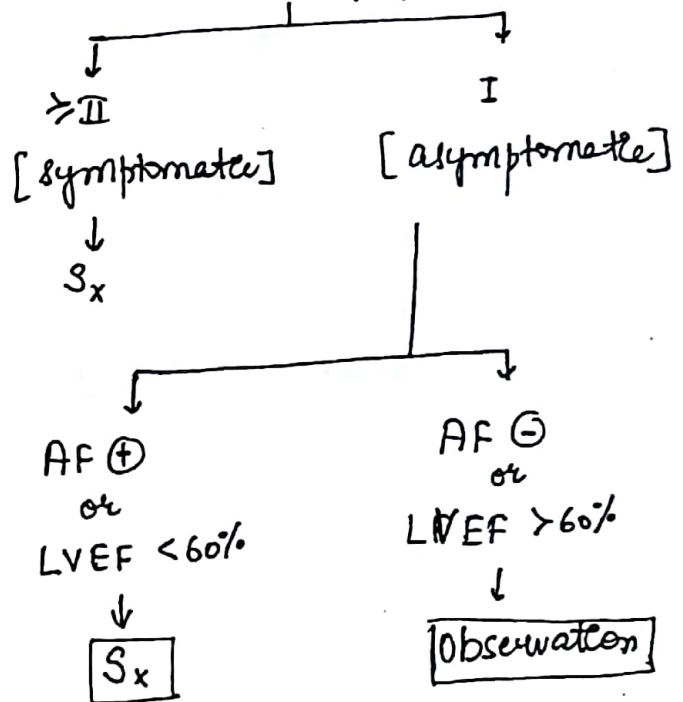
③ - 4-6 cm^2

NYHA symp



Severe MR

NYHA symp

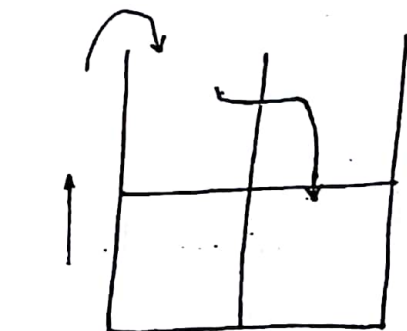


Sx

Preferred Sx / Initial Process of choice / Sx in ⊕
Balloon valvotomy

Preferred Sx = MV Repair

If not possible
↓
MV Replacement



IVC
Done under Lung-Heart Bypass machine.

Criteria:

- 1) Isolated MS
- 2) no calcification
- 3) no LA Thrombus

↓ if not fulfilled

MV Replacement

↓

Metallie	Bioprosthetic
----------	---------------

Dur. 25yrs 5-10yrs

Anticoagulation X
= lifelong

Age Preference
= young elderly

Q. 26yr old, unmarried ♀. K/c/o RHD & MS
c/o - dyspnoea on 10 steps. Echo = MVA 0.8cm^2 .

Next Line Rx

- a) observation
- b) balloon valvotomy
- c) Bioprosth, MV replacement
- d) Metallie, MV "

Q. same history. O/E - opening snap (+ve.)

Ans - (b)

Q. same history, O/E - $\frac{\text{Pulse Defect} + 20}{\text{AF}}$, opening snap (-nt) Calcification.

Q. Same history. marvelled QE - opening snap (-), MR (+)

66

ans → (d)

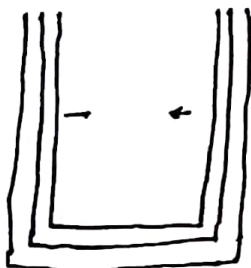
↓
(b)
↓
Give heparin in 1st Trimester
anticoag in 2nd Trimester - 3rd
heparin in 3rd " delivery.
2 wks prior to.

AS

Cause - M/c age related calcification

Pathophysiology:-

LV pressure overload
↓ remodelling



LV (concentric) Hypertrophy

↓ later

LV systolic failure

↓
LA 'P' ↑

AR

M/c - age related degeneration

LV volume overload.

↓ remodelling



LV (eccentric) Hypertrophy

↓ later

LV systolic failure

↓
LA 'P'

Symptoms:-

Mech.

17 Due to

17 Angina ← ↑ LV work load 17 Palpitations ← LV force of contraction ↑

2) Syncope ← Fixed CO

3) Dyspnoea ← LA 'P' ↑
[Worst Prognosis]

Mortality \bar{c} in $1\frac{1}{2}$ yr even \bar{c} medical t/t

Signs:-

→ Pulse - Most specific
Parvus et tardus

⇒ Apex - LV 'P' overload

↓
Site = (N)

Nature = Sustained

3) S_1 = Soft

S_2 = split = reverse

Lvejer time ↑ → Late A_2

in early stages → narrow split

S_3 = + if LVF occurs

S_4 = ++

Ejection click = (+)

2) Angina [Nocturnal]

← ↓ in Diastolic BP \bar{c} lead
to less perfusion

↓
This occurs more during night
as sympathetic activity ↓
further ↓ vascular tone.

3) Dyspnoea ← LA 'P' ↑

Most specific.
= Bisferiens

LV Dilated + vol. overload

Site = Shifted Laterally

Nature = Hyperdynamic

S_1 = Soft

S_2 = Single P_2 .

aortic valve leaflets
fail to strike.

S_3 = ++

S_4 = + Late AR.

(-)

47 1° Murmur

Type = Ejection Systolic murmur

Type = Early diastolic

68

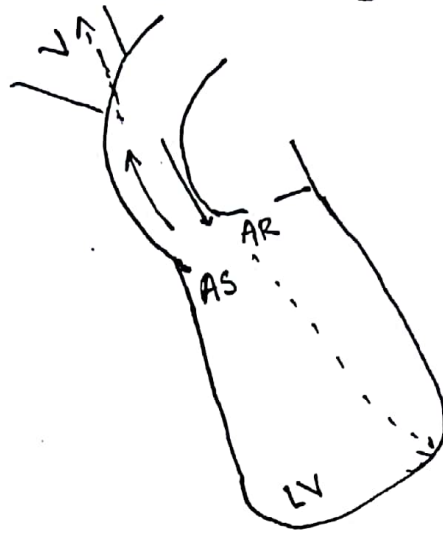
Site = (R) 2nd ICS [Aortic area - 1st]

Site = (L) 3rd ICS [Emb's Area]

2nd Aortic Area

or

Neo-aortic area



Pitch = Low

Pitch = High

Radiation = Common carotid
[or neck]

Radiation = towards apex

after striking arch of aorta
radiation to apex

if radiation to axilla

= GALLAVERDIN PHENOMENA

= COLE - CECIL MURMUR

Best Pt's Position =
Leaning forward. ✓

Phase - expiration ✓

2° Murmur

Not seen in AS

1> Austin-Flint murmur
mid-late diastolic

2> Functional AS

T. Blood flow across
aortic valve

[Ejection Systolic]

Clinical Criteria for Severity

- 1) S_1 = Soft
- 2) S_2 = Reverse split
- 3) S_3 = (+)
- 4) S_4 = (+)

* Severe Silent AS

- 27 associated MS
 - 27 LVF
- ↓ CO
↓
Hence sound ⊖

I_x

[ECG] = sequence

① LVH signs



② LA enlargement



ST Depression
T inversion → strain pattern

[CXR]

Cardiac Size = (N)

R_x

Similar
Severe AS or Severe AR

[Area $< 1 \text{ cm}^2$]



NYHA symptoms

≥ II (symptomatic)

I (asymptomatic)

17 Any peripheral sign of AR

27 Pulse - Bisferian

37 Apex - Displaced Laterally

47 S_1 - Soft

57 S_5 - (+)

67 1° murmur = Duration.

77 Presence of 2° murmur
= Austin-Flint murmur

[ECG] = sequence

① LVH



② LA enlargement



ST Normal
T upright as inner myocytes
receive blood
from cavity

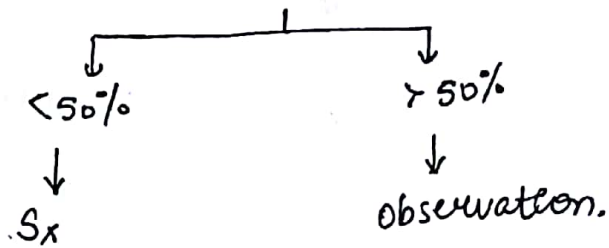
[CXR]

enlarged

↓
S_x

↓
LVEF

70



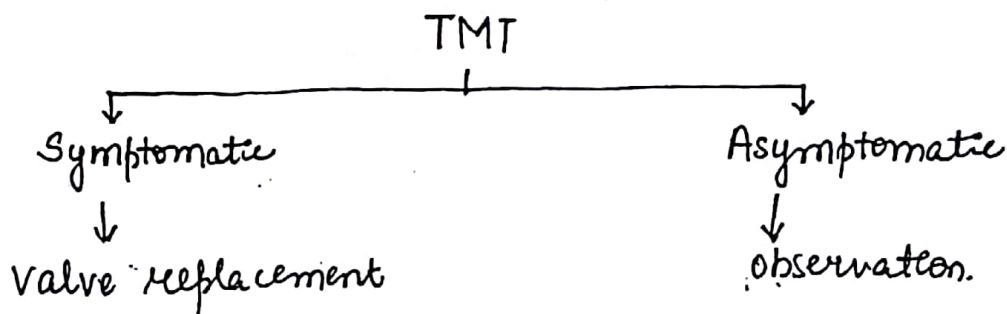
Preferred S_x = Aortic Valve Replacement

Q. 60yr old ♂, \bar{e} Aortic valve pressure gradient of 60 mmHg.
K/a/o AS, c/o - equivocal dyspnoea symptoms
Next step?

- Ans.
- a) observation
 - b) Tread mill test
 - c) Aortic Valve Replacement
 - d) Diuretics.

Q. Same pt. underwent treadle mill test [Bruce Protocol]
c/o Dyspnoea & Fatigue at 11 min of exercise
Next step

Ans.



Bruce Protocol

Bruce stage

I

II

III

IV

Duration

71

0 - 2:59 min

3 - 5:59 "

6 - 8:59 "

9 - 11:59 "

Pt. considered symptomatic if % dyspnoea / % of fatigue

≤ Stage II

Asymptomatic if % dyspnoea / % of fatigue

≥ Stage IV

* Severe AS + NYHA-I + underlying CABG = Aortic valve Replacement

(R) SIDED VALVULAR LESIONS

Lesion	M/c Cause	Other causes
1) TS	RHD	(x)
2) TR	RV dilatation. [eg. Pulmonary embolism] cor-pulmonale	M/c Valvular Lesion due to CARCINOID
3) PS	Congenital	Carcinoid Rubella
4) PR	Pr PAH	Carcinoid

Valve fibrosis → Regurgitation

Ring fibrosis → Stenosis

LMR INFECTIVE ENDOCARDITIS

72

CAUSE :-

Predisposing Causes

1> M/c Valvular Lesion = MR > AR.

2> M/c congenital HD = VSD [R ventricle has vegetation]

3> M/c cyanotic cong. HD = TOF [L ventricle has vegetation]

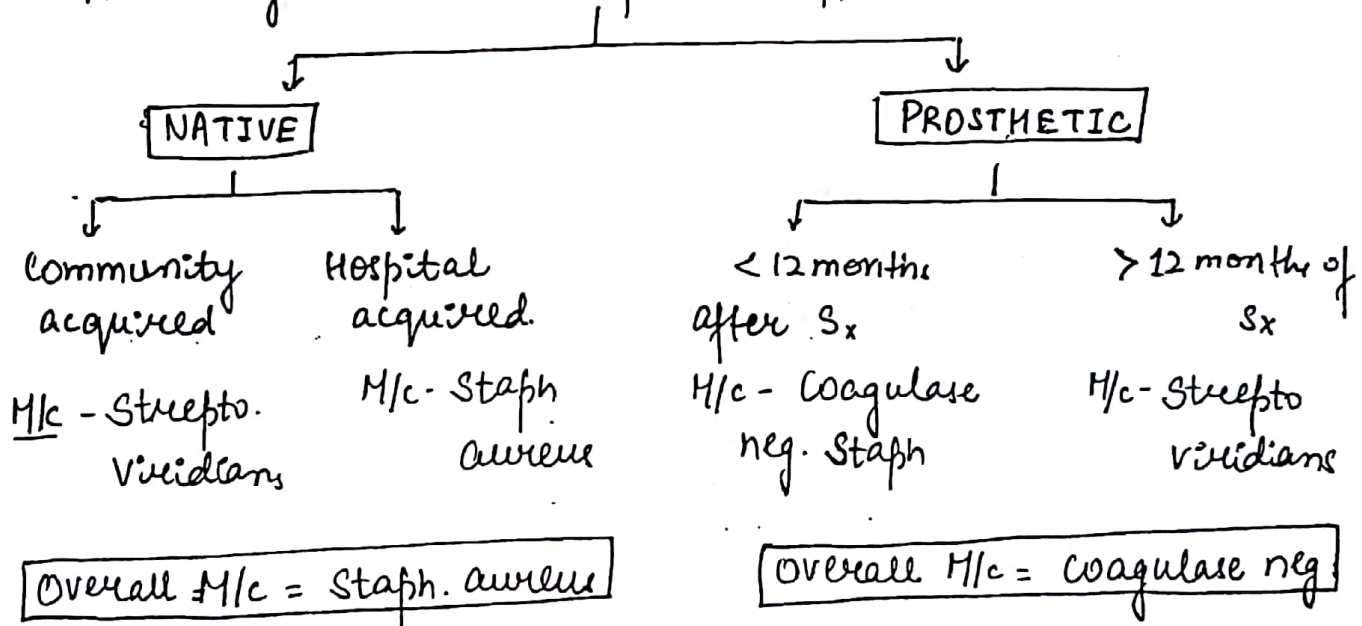
↳ systemic embolism.

4> Least common HD leading to IE = ASD

5> MC non-CV risk = " " " = IV Drug Abuse

Micro-organisms

* According to nature of valve affected.



Max incidence = 6-12 months

HIV is the only virus to cause IE.

* According to Onset of

73

Acute

[<2wks]

M/c = Staph aureus

Other

Strepto β -haemolytic

Fungus

Subacute

[>2wks]

M/c = Strepto. Viridians

Other

Staph coagulase neg.

Fungus

* Typical Bacteria of IE

1) Strepto Viridians

2) " Bovis [Gallolyticus] \rightarrow ass/c Colonie cancer/ Polyp.

3) Staph aureus \rightarrow M/c in IV Drug Abuse \rightarrow (R) sided

4) Enterococci \rightarrow M/c in IV Drug Abuse \rightarrow (L) sided.

5) HACEK group

C/F + Ix

Modified DUKE'S Criteria

2 MAJOR

5 MINOR

3 EXCLUSION

* Major Criteria -

(I) Evidence of micro-organisms consistent c IE.



1) ≥ 2 Blood culture (+) of Typical Bacteria

OR

2) Persistent Bacteremia of micro-organism consistent c IE.

OR

≥ 2 Blood culture (+)

[separated by 12 hours]

≥ 3 Blood culture (+)

out of ≥ 4 samples

[1st & Last sample separated by 1hr]

37 > 1 Blood Culture } of *Coxiella Burnetii*
or
IgG \uparrow

74

(II) Evidence of Endocarditis [ECHO]

\downarrow
ECHO ① Oscillating Mass Lesion on valve or its structure

or
② Intra-cardiac abscess

OR
③ New valvular regurgitant lesion \leftarrow M/C CVS complication of IE.

OR

④ Partial Dehiscence of prosthetic valve

* Minor Criteria

1) H/O Predisposing cause = RHD, I.V. Drug Abuser.

2) Fever $> 38^{\circ}\text{C}$ \leftarrow M/C Symptom

3) Immune phenomena = RRO4

R \rightarrow Roth's Spots \rightarrow Immune complex vasculitis in Retina
Oval
Pale centre, \bar{c} haemorrhagic margins



Other causes -

a) SLE

b) CLL

\Rightarrow

O \rightarrow Osler's Nodes \rightarrow Immune complex deposits in
Finger tips / Palms / Soles.
Tender
Palpable

G₁ → GN → Immune complex deposited in
S. C₃ levels ↓

75

R → RA factor +ve

47 Vascular Events

* Major Arterial Embolisation

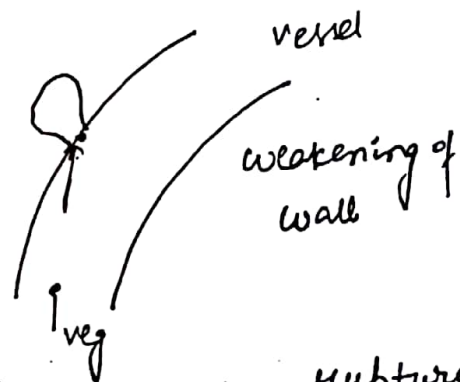
[L sided] M/c site → Brain [MCA territory → Parietal]
→ Spleen

M/c organism → Staph Aureus

M/c Valvular IE → Mitral valve

* Septic Pulmonary Infarcts
[R sided].

* Mycotic aneurysm



* Haemorrhagic stroke [if mycotic aneurysm rupture in Brain]

* Conjunctiva petechiae.
M/c Peripheral sign of IE.

* Janeway Lesion = Palms.
Macular [non-palpable]

Non-tender

57 Blood Culture Positive of micro-org consistent = IE
(not satisfying major criteria)

or

Serology +ve

Definitive Δ of IE = 2 Major
or

76

1 Major + 3 Minor
or

All 5 minor

* Exclusion Criteria

- 1> Firm alternate Δ of Fever established.
- 2> If fever subsided in 4 days of Antibiotic Use.
- 3> If there is no histopathological evidence of IE < 4 days of Antibiotic Use.

R_x + Prophylaxis of IE = given in supplement.

14/2/18

CARDIOMYOPATHY

77

Definition:-

Diseases of endomyocardium

Not due to valvular Heart disease.

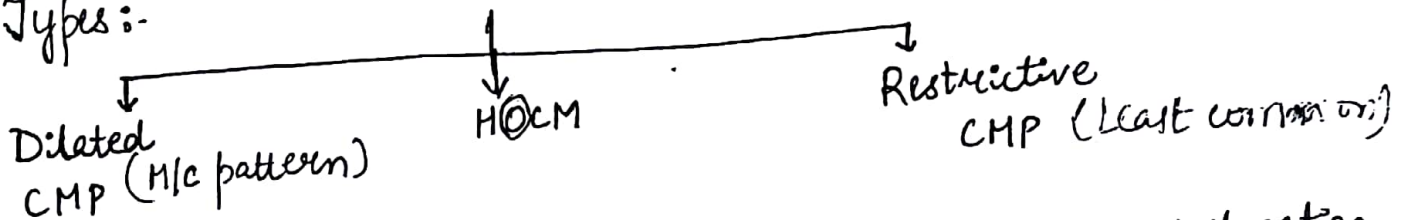
27 Cong. Heart disease

37 HTN

47 Ischaemia

57 Pericardial Disease

Types:-



Defect:-

↓ contractⁿ

↓

↓ in systolic funcⁿ

+

Preserved diastolic funcⁿ till late stages

Obstructⁿ to LV outflow
↓ overcome obstructⁿ

↑ in systolic funcⁿ

+

(↓ cavity space)

↓ diastolic funcⁿ

Failure of relaxation

↓

↓ in diastolic funcⁿ

↓

Systolic funcⁿ preserved.

Gross atrial Dilatation

DILATED CMP

CAUSE-1 Idiopathic (M/c cause)

R_x - Supportive. [chr. HF = low EF]

2^o cause - alcohol

Mech:- a) Direct ethanol effect

b) Becoz of Cobalt [cardiotoxic agent]

↓
(foam stabilizing agent)

Risk :- Mutation of alcohol dehydrogenase
 • Mutation of ACE (?)

Dose of alcohol :- $\geq 120 \text{ gm/day}$ for $5-10 \text{ years}$

R_x = reversible in $3-6 \text{ months}$ of cessation.

Other CVS manifestations of alcohol ($> 30 \text{ g/d}$)

1) Dyslipidemia

a) $M/C = \uparrow TG$

b) $\uparrow HDL C$

c) $\uparrow LDL$

Ethanol

$\downarrow \ominus$

FA metabolism

\downarrow

$TG \uparrow \leftarrow FFA \uparrow$

2) Effect on BP

Acute - vasodilatation = $\downarrow BP$

Chronic - \oplus sympathetic system = $\uparrow BP$

3) CVS events

a) CAD \rightarrow \downarrow risk by $\uparrow HDL$ [French paradox]

b) stroke \rightarrow \uparrow risk due to $\uparrow BP$

c)

4) Arrhythmia

alcohol binge \rightarrow AF [Holiday Heart Syndrome]

III) Genetic Causes

MOI

17) AD

Q. Gene/Protein

TTN / Titin

↓
sarcomere protein. (N)
helps in contract

Unique feature
79

M/c genetic cause of
DCMP

27) AR

DSP / Desmoplakin

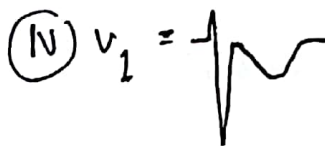
↓
Desmosome protein
(N) helps in synchro.
contract

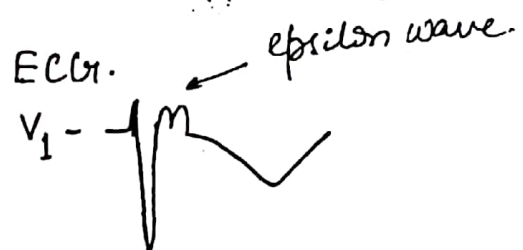
Arrhythmogenic
RV Dysplasia. (ARVD)

↓
Sudden cardiac death
in young population.

NAXOS
Disease

- {wooly hairs +
thick palmar skin +
ARVD

(N) $V_1 =$ 

ECG. $V_1 =$  epsilon wave.

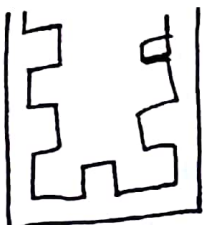
3) X-R

TAZ / Tafazzin

↓
(N) helps in compaction
of ventricle cavity
during embryonic
development

LV non compaction.

* LV thrombus since
birth.



Embryonic



IV Post Myocarditis

80

A Causes :-

Infectious

1) MC viral - Coxsackie B

other viral infectⁿ

- Parvovirus B19

- HIV

- Hepatitis C

Non-infectious

1) MC - Sarcoidosis [lung involvⁿ]

MC site → LV free wall

MC pattern → DCM > RCM

R_x = steroids

2) Bacterial

MC - Diphtheria [death by myocarditis]

R_x - anti-toxin

2) Giant cell Myocarditis
(no lung involvement)

R_x - steroids.

3) Protozoa

MC - Trypanosoma Cruzi
[Chagas Disease]

R_x - Benznidazole

3) Hypersensitivity Myocarditis

cause - Thiazide

Indomethacin

Methyldopa

4) Parasite

MC - Toxoplasma

R_x - albendazole

R_x - cessation of drug
± steroids

Q V. Tako-Tsubo CMP / BROKEN HEART SYNDROME / APICAL BALLOONING SYNDROME

C/F - ♀ + ↑ catecholamine release
↓
vasoconstriction of LV apex
↓
LV apex non-contractile
↓
During systole RV apex bulge out in systole
like balloon.

Ix - ECG - STT

Troponin = ↑ or (N)

coronary angiography → no thrombus

ECHO - LV apex bulging out in systole.



→ resembles a jar used to trap octopus
↓
hence called Tako-Tsubo.

Rx - reversible, so supportive therapy
+ α blocker followed by β blocker [like phaeochromocytoma]

VI . Peri- Partum CMP

Mech:- 1> Autoimmune damage to myocytes by foetal Ag⁸².
2> Prolactin fragments → myocyte damage

C/F:- occur in 3rd trimester - 6 months post delivery

Risk ↑ → Twin Delivery
multipara
age > 30 yrs

Rx - 1> Diuretics

2> Bromocriptene [by ⊖ Prolactin].

└→ also used in Type 2 DM.

RESTRICTIVE CMP

83

Pathology :-

Infiltration

Fibrosis

(I) Infiltration

A> In between myocytes

eg. Amyloidosis

M/cc of RCMP



Types

1> 1° amyloidosis

Protein/cause

AL/multiple myeloma

Waldenstrom macroglobulinemia

NHL

CF

Age - > 50 yrs

M/co organ - Renal

M/cc = CVS of death

unique - Black or Raccoon eyes.

Rx

underlying disorder.

Factor Xa adsorbs on AL protein leading to ↓ in blood

blood def. of Xa. [ecchymosis]

2> Familial

Trans thyretin [liver]

↑ genetic

Age > 20 yrs

M/c = CVS organ

M/cc of - CVS death

unique = ascending neuropathy

1) Liver Transplant

only cond where liver

Transplantation is done out

Liver failure

2)

New Rx

TAFAMIDIS

84

↳ stabilizes β transthyretin

37 Senile
Cardiac
Amyloidosis

Transthyretin
2 Age.

Age > 70 yrs

Tafamidis

M/c organ }
M/c of death } - CVS

* 2° amyloidosis doesn't cause left ventricular CMP

* ECG will show Low voltage QRS as amyloid is poor conductor

* Echo = \uparrow ventricle wall QRS

(B) Infiltration Inside Myocyte.

1) Haemochromatosis

M/c pattern \rightarrow DCM $>$ RCM
of CMP

M/c of death in untreated pt \rightarrow CVS

M/c of death in treated pt \rightarrow HCC

Rx - Phlebotomy \rightarrow [CMP is reversible]

2) Fabry's Disease

Cause - Defⁿ of α -galactosidase
 \downarrow
Glycosphingolipids accumulate

CF.

85

- 1) CVS → RCMP
- 2) Kidney → (GBM damage)
3rd H/c systemic cause of Nephrotic Syndrome
- 3) Abdomen - Angiokeratoma Q

Ix - Kidney Bx = GBM. ≡≡≡ zebra Bodice
(electron microscopy)

Rx Recombinant Galactosidase. [stop the progression of Ds]

(II) Fibrosis

1) Radiation [Ca breast/lungs] } Supportive Rx.

2) Systemic sclerosis

3) Loeffler's Endocarditis

Eosinophilia

Release of ↓ Basic Protein.

Fibrosis

Rx - Steroids (by ↓ eosinophils)

CHF

86

ACUTE HF

↑
Acute MI
HT
Arrhythmia
IE

CHRONIC HF

↓
Low EF [$<40\%$]

↓
CO will reduce
Systolic failure

↑
eg. DCM
Late AS, AR, MR

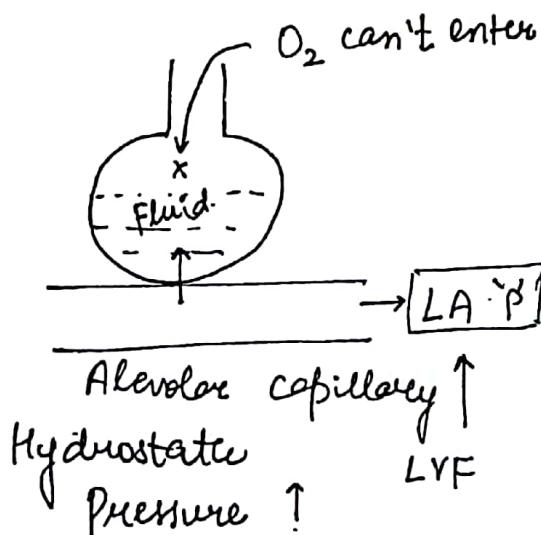
↓
Preserved EF
[$>40-50\%$].

Diastolic failure

↑
eg. HOCM.
RLMP
Ageing Process

Rx of Acute HF :-

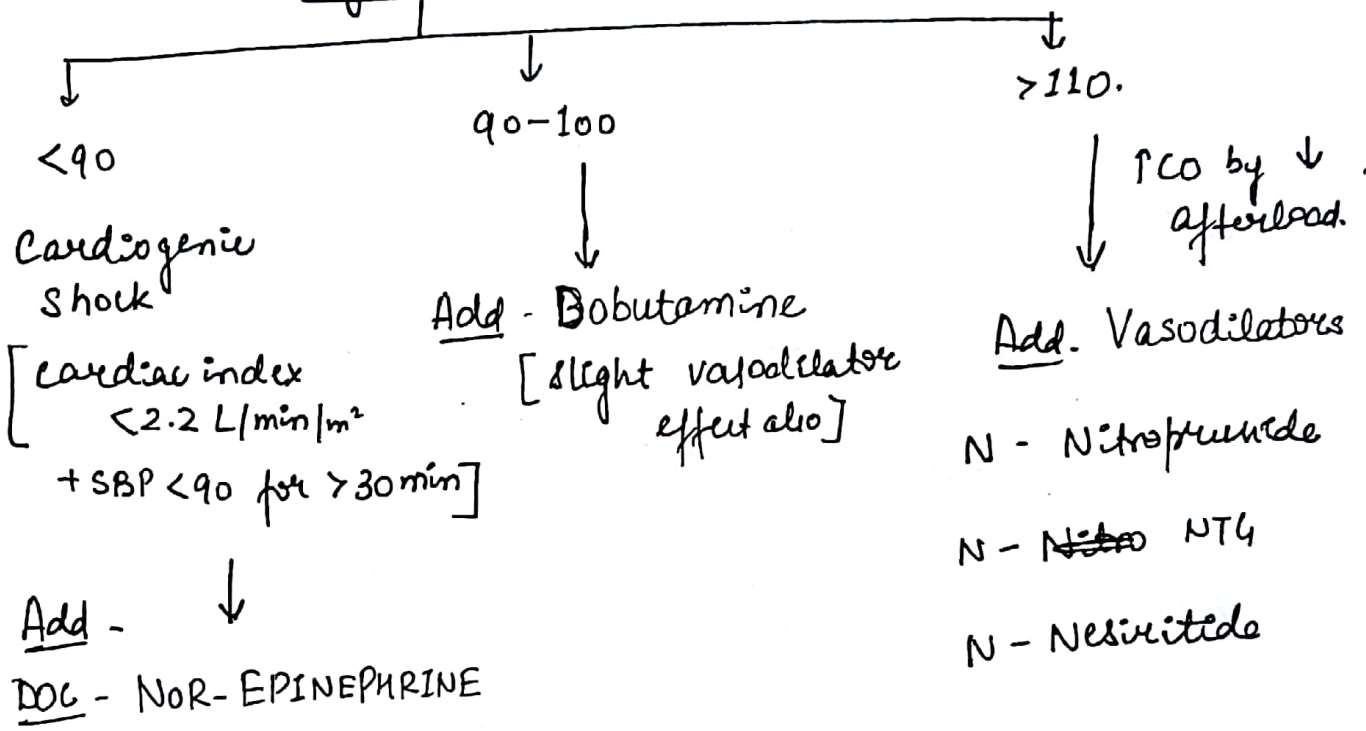
Acute HF = Acute cardiogenic Pulm. edema



AIM OF Rx - Shift alveolar fluid into capillaries
↓
by ↑ capillary hydrostatic pressure
↓
Achieved by ↓ R sided Preload

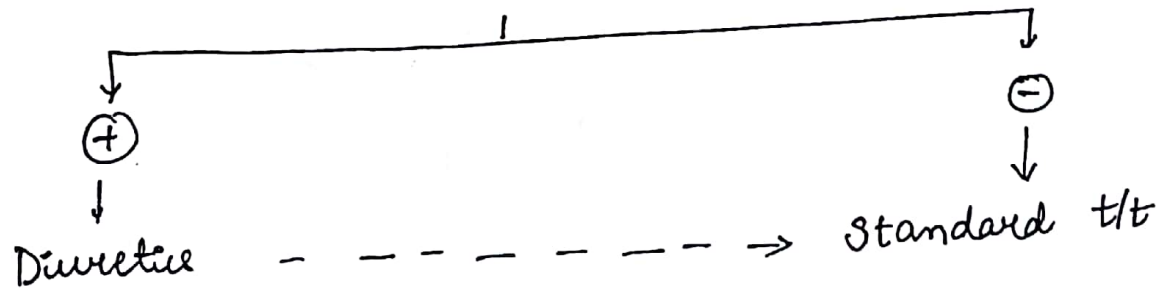
1> Diuretic [Furosemide] ← Initial Rx
 +
 2> Morphine [venodilator]
 +
 3> O₂ inhalation.

↓
 [Systolic BP]



Rx of Chv. Heart Failure ⊂ ↓ EF.

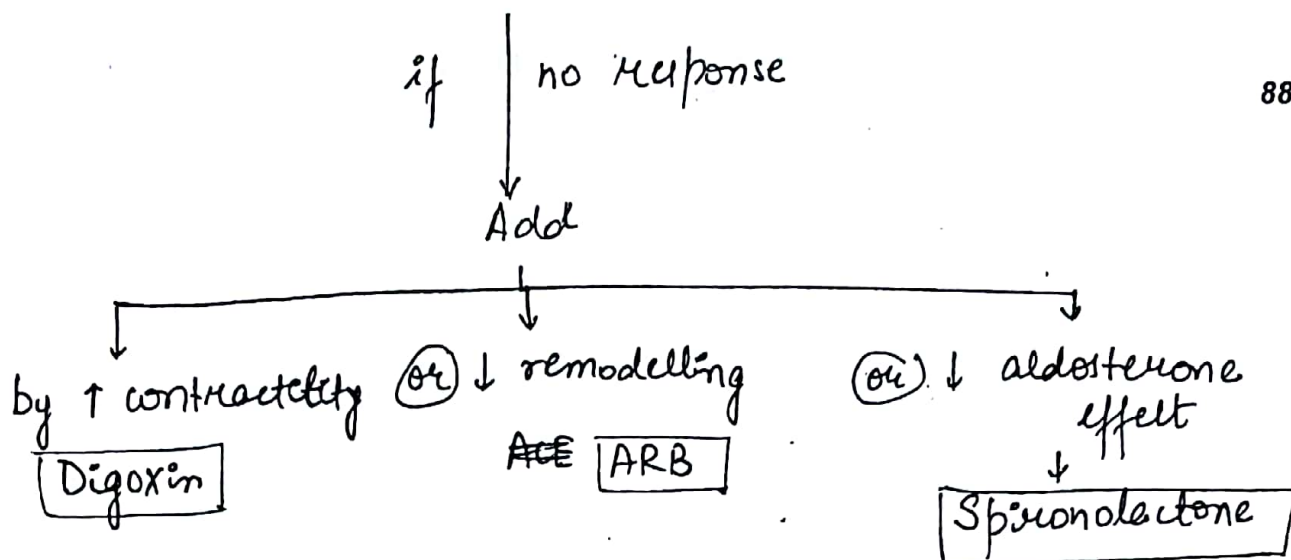
↓
 Fluid Overload



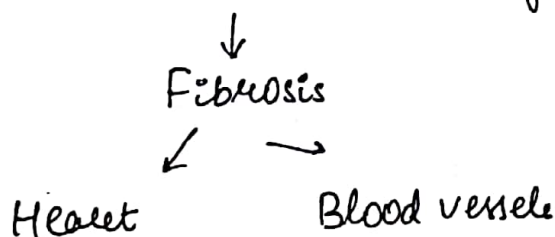
1> ACE Inhibitors.
 By ↓ remodelling + ↓ afterload.

- a> Metoprolol
 - b> Carvedilol
 - c> Bisoprolol.
- ← vasodilator also

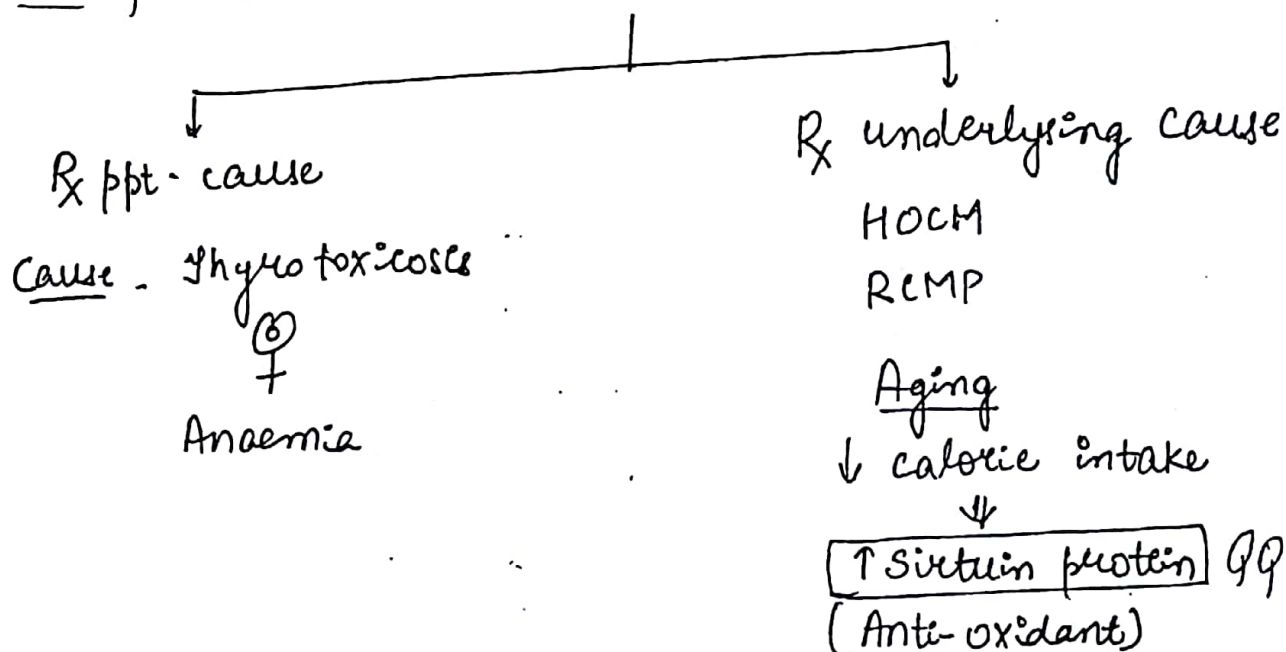
+
 2> β blocker
 By ↓ workload + ↓ sympathetic activity



Chr. ↓ CO → Chr ↑ aldosterone (by (+) RAAS)



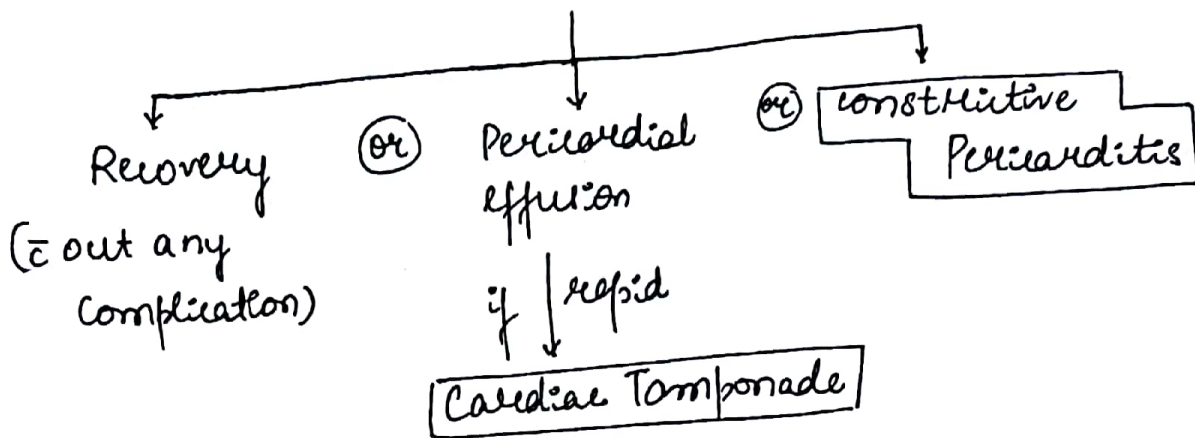
Rx of Chr. HF with Preserved Ejection Fraction



PERICARDIAL DISEASES

89

Acute Pericarditis



ACUTE PERICARDITIS

Cause - M/c - Idiopathic

Symp - M/c - chest pain [due to rubbing w/ mediastinal pleura]

Ac. Pericarditis

Site - M/c Retrosternum

Nature - sharp pain

Radiation - Trapezius

Aggravating factors - Supine
(as area of contact w/ pleura ↑)

Relieving factors - Leaning forward
Not relieved by nitrate

Ischaemic Pain

Retrosternum

Dull/constricting

Never sharp

① arm, forearm

Never Radiate to Trapezius

Exertion

Cold Temp

Rest

Sublingual nitrate

Sign - Most Specific \Rightarrow Pericardial Rub.

90

- Crackling sound due to rubbing of 2 inflamed pericardial layers
- Diastolic Phase

Ix

ECG :-



PR segment depression +
ST concave upwards ST elevation
[Smiling Phase ST elevation]

Stage of Ac Pericarditis

I



ST \downarrow + PR segment \downarrow or remains \downarrow

II



III

T wave inversion



IV

\odot ECG [recovery phase]

ECG

Ac. Pericarditis

① ST ↑ concave upward

② ST ↑ seen in all leads.
almost except - ~~area~~
aVR, V1

③ ST (N) followed by T inversion

④ +ve of reciprocal ST depression in opp. wall lead

⑤ Pathological q wave

[indicate myocardial necrosis]

Ac. MI

91

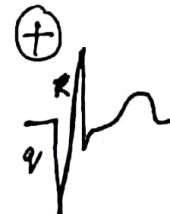
convex upward.

specific lead

T inversion occur before T normalise



(+)



Deep q wave

depth > 25% of R wave
+
Duration > 1mm.

Rx - 1) underlying cause
2) Idiopathic.

DOC → NSAIDS

↓ no response

Colchicine

anti-inflammatory +
anti-fibrotic

→ steroid
no response

TAMPONADE

Cause - M/c (world) - idiopathic

M/c in India - TB

Pathophysio - Acute

"Compression" of heart +
venous roots + Aortic roots

↓↓
↓↓ venous return (40-50ml) ↓↓ CO

Compensatory vigorous
ventricle contraction to
maintain CO.

Obstructive
or shock
Compressive

Symptoms -

M/c → Dyspnoea due to
↓ in MHP. M/s
perfusion

* Not due to Pulmonary
congestion.

Lungs - Oligemia

Signs -

Pulse - Pulse Paradoxus
≥ 90% cases

⊖ in Tamponade

CONSTRICTIVE PERICARDITIS

92

Idiopathic

TB

Chronic

"Failure of relaxation" of
heart due to stiff Pericardium
+ CO is preserved

↓↓
↓ venous return (100ml)

Compensatory vigorous
ventricle contraction
to maintain CO

M/c → Swelling

due to chr. ↓ in venous
return.

↓
Hydrostatic 'P' ↑ in systemic
veins

≤ 1/3rd cases

Absent Pulsus Paradoxus in Tamponade

93

- 1> AR Tamponade
- 2> CHF

JVP Deep x

Vigorous RV
contraction
↓
The cupped ring
pulled downward

Deep x

Y = Absent

Y = Rapid

a = Prominent

U = Prominent [failure of relaxation of RA]

Kussmaul = ⊖
Sign as venous return
doesn't ↑ significantly
in Tamponade

⊕

Apex - Non-Localised

Non-Localised

S₁/S₂ soft

soft

S₃/S₄ ⊖


⊖

Pericardial knock ⊕
[3rd HS]

Ix

⊙ CXR - ↑ cardiac shadow
(Not true cardiomegaly)

CXR - cardiac size normal
+
calcified pericardium

 ← Margins smooth.
+
Lung field oligemic

27 ECG =

QRS amplitude ↓

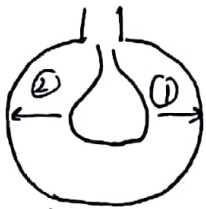
[Electric alternans]

ECG

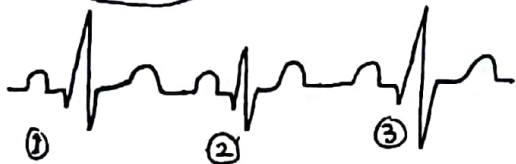
QRS amplitude ↓

94

[Non specific ST ↓ or T ↓]



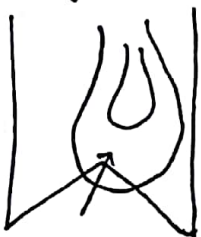
1 = ECG lead.



R_x

Emergency Pericardiocentesis

Routine - Pericardiectomy



[ECHO]

Needle [Subxiphoid area]

Signs

Description

Best Δ

1> Auerbach's Sign

Epigastric Bulging

Massive pericardial effusion

2> Beck's Triad

↓ BP + ↑ JVP +
Soft HS

Tamponade

3> Ewart's Sign.

compress (L) side
airway

Massive Pericardial
effusion

collapse of distal lungs

↓
Bronchial Breath Sound

(L) Infrascapular area

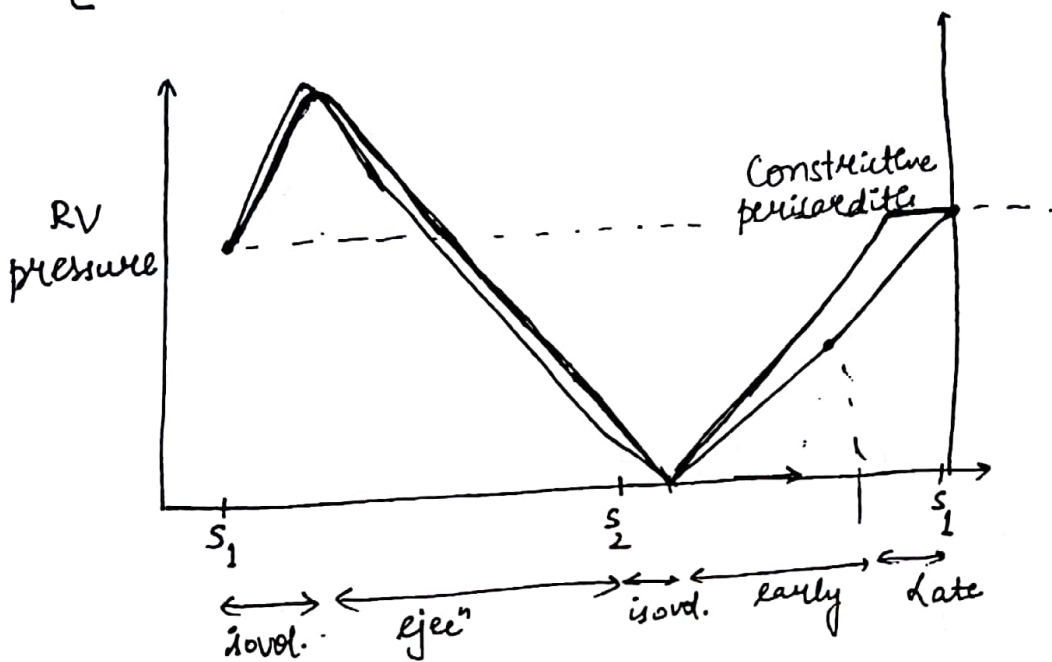
4) Broadbent's sign

systolic retraction of apex
due to fibrous pulling

Constrictive Pericarditis.

"Square root" sign
[Pressure changes in RV]

→ Constrictive Pericarditis.



LMR

SYSTEMIC HTN

96

Classification [AHA guidelines Nov 2017]

SPP

DBP

1) Normotensive	<120	AND	<80
2) Elevated	120-129	AND	<80
3) Stage I HTN	130-139	(OK)	80-89
4) Stage II HTN	≥140	(OK)	≥90

Causes

I. Essential / 1° HTN (no identifiable cause)
M/c cause

II. 2° HTN (identifiable cause)

↓

1) M/c 2° cause - Reno-Parenchymal
[GN, Chr KD].

M/c Mech → vol. overload

2) 2nd M/c → Reno-Vascular
[Renal artery stenosis]

Mech - ⊕ RAAS

DOC - ACE-I in U/L stenosis

3) Activating Mutation of Sodium channel of tubules.

↓
DCT - Na⁺ channel

Δ GORDEN'S SYNDROME

↓
CD = 2 Na⁺ channel

Δ - Liddle's Syndrome

Doc - Thiazide

Doc = Amiloride.

97

47. Endocrine causes.

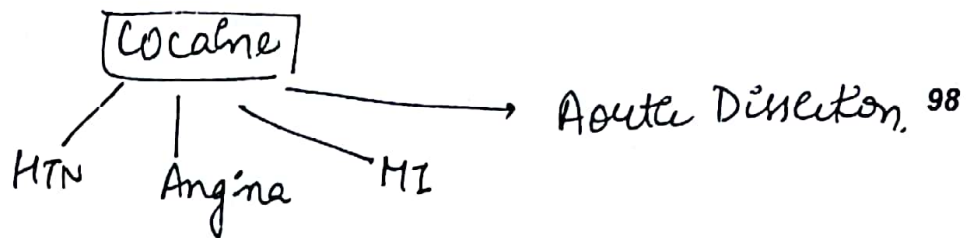
<u>Endocrine</u>	<u>Type of HT</u>	<u>Edema</u>
a) Hypothyroid	DBP ↑ (compress bld. vessels)	⊕ Myxoedema
Conn's Syndrome b) chr. ↑ aldosterone ↳ vessels fibrosis	DBP ↑	⊖ ANP released ↓ "Escape" Mechanism
c) <u>Hyperthyroidism</u>	SBP ↑ (due to ↑ CO)	⊖
d) <u>Phaeochromocytoma</u>	SBP + DBP ↑ sustained HT > episodic HT	⊖

57 Miscellaneous Causes

- a) M/c Cong. CV cause of HTN ⇒ Coarctation of Aorta
- b) Systemic HTN $\xleftarrow{\text{sympathetic } \uparrow}$ Obstructive sleep Aпноea
- Pulm. HTN $\xleftarrow{\text{hypoxia}}$

c) PCOD = Insulin resistance
[acanthosis nigricans]

d) Drug NSAIDs by ↓ GFR
Corticosteroids
estrogen



Symptom

1) M/c - Dyspnoea [due to CHF]

M/cc of CHF = **HTN**

2) M/c Symp due to HTN → Occipital Headache

3) **Sign** 1) $LV S_4 +$ (due to LVH)

I_x -

ECG Change

1) LVH signs

2) LA enlargement

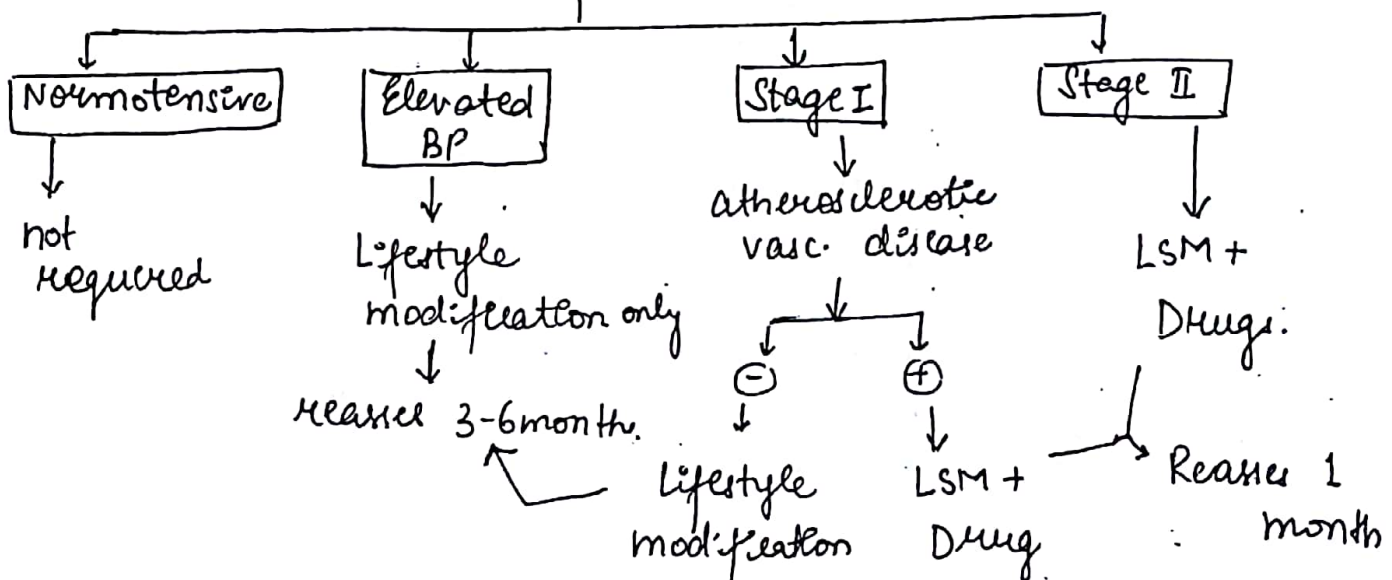
3) LAD

R_x

Stable

≥ 2 Reading on ≥ 2 occasions
should be ↑ to Δ HTN

R_x



* Lifestyle Modification

- 1) wt. reduce
- 2) \downarrow Na $\leq 1.5\text{gm/day}$
- 3) \uparrow K $3.5-5\text{gm/day}$ cause smooth M/s Relaxation

4) DASH DIET

Dietary Action To Stop HTN

\downarrow Na⁺ \downarrow Fat dairy product,
 \uparrow Fruits & veg. \downarrow Saturated fat

5) Brisk Walk / Exercise $\geq 150\text{ min/wk}$

6) Alcohol $\sigma < 30\text{g/d}$ $\phi < 15\text{g/d}$

Other Terms

1) Resistant HTN

If BP $\geq \frac{140}{90}$ despite ≥ 3 drug (one of \leq is diabetic)
 or

If BP $< \frac{140}{90}$ \bar{c} ≥ 4 drug

M/c \rightarrow Non-compliance

2) White Coat HTN

In clinic If SBP > 20 σ or DBP > 10 from non clinical readings.

3) HTN Emergency = If $\boxed{\text{BP} > 180/120}$ \bar{c} Target Organ Damage
 \downarrow

I.v. Labetalol

\leftarrow 1) Haemorrhagic Stroke

I.v. ~~Nitro~~ NTG or
 Nifedipine

\leftarrow 2) Ac. cardiogenic Pulm. Oedema

I.v. NTG

\leftarrow 3) Ac. MI

I.v. Esmolol

\leftarrow 4) Aortic Dissecⁿ

Nimodipine

\leftarrow 5) SAH

* Mean BP reduction \rightarrow 25% from presentation value
 $\left[\text{DBP} + \frac{1}{3} \text{PP} \right]$ $< 1-2$ hrs. 100

* DOC for HT Emergency = I.V. Nicardipine

* 4> HTN Urgency = $\text{BP} > \frac{160}{120}$ + no target organ damage

R_x = combination of oral drugs.
[OPD]

5> Orthostatic Hypotension

if SBP \downarrow by > 20] in 3 min of standing
 DBP \downarrow by > 10]

M/c cause \rightarrow Hypovolemia

2° HTN associated w
 ortho static HTN

= Phaeochromocytoma

chr. vol. depleted

\uparrow
 due to chr. vasoconstriction

IHD

101

	Stable Angina	Unstable Angina	Non-ST ↑ MI (Subendocardial)	ST ↑ MI [Transmural]
Duration	2-10 min	20 min	20-30 min	> 30 min
Pain at rest	(-)	(+)	(+)	(+)
ECG at rest	(N)	ST depression [except Prinzmetal Angina]	ST depression	ST elevation.
Troponins	(N)	(N)	(↑)	(↑)

Symptoms M/c → chest pain
Painless MI → "Autonomic Dysfunction"
[DM, elderly]

↓
'Angina' equivalent symptoms
a> unexplained sweating
b> " Dyspnoea
c> sense of impending Doom

Signs M/c → LEVIN SIGN [Holding Palm or Fist against sternum]

Pulse - if tachycardia = Ant. wall
Bradycardia = Inf. wall

JVP - if Kussmaul sign = RV MI.

S_2 = if split is wide = RVI [late P_2]

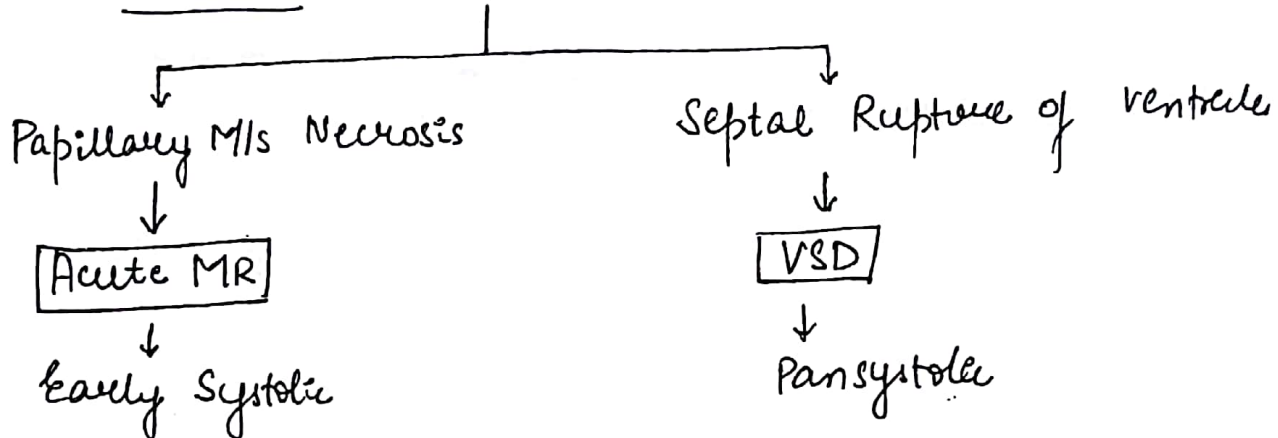
if split is reversed = LVI [late A_2]

poor prognosis S_3 - if $(+)$ → indicate systolic failure
[Infarct > 40%]

S_4 - $(+)$

[more common than S_3]

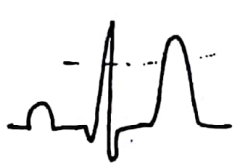
Murmurs -



ECG

Sequence of changes

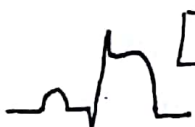
1>



Tall T Wave

(> 50% of R wave height)

2>



ST T (convex)

Pandey Sign

3>



T↓

Mech

Leakage of K^+

[Similar to hyperkalemia]

Early Repolarisation of infarcted m/s

Non-specific

4)



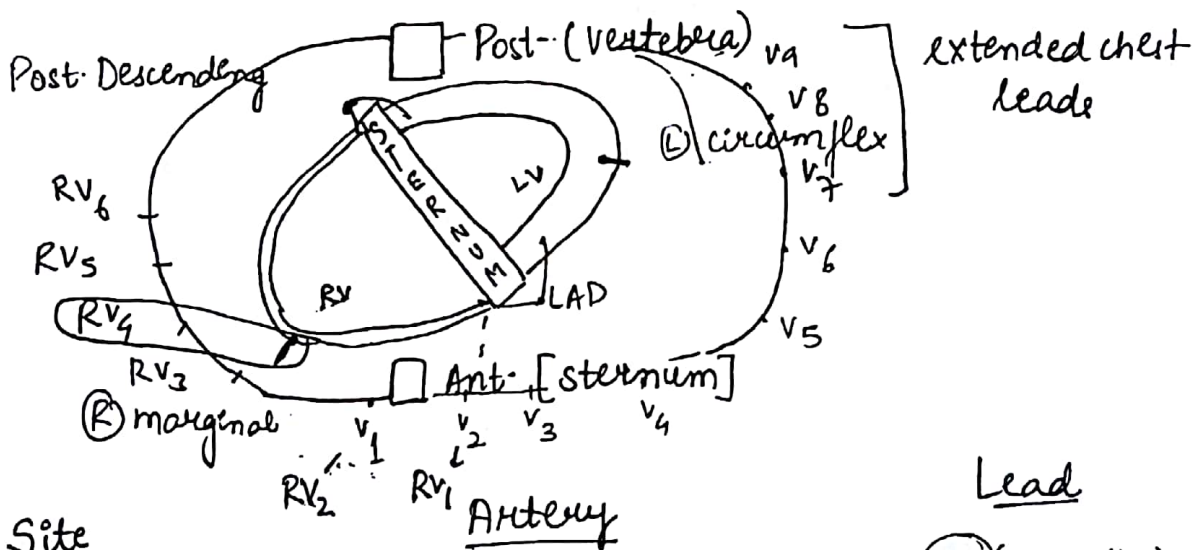
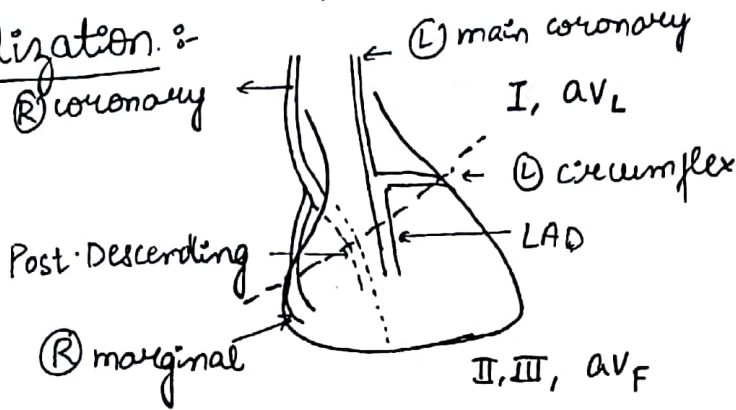
Pathological Q wave

Neurosis

103

NO use of thrombolytic therapy

Localization:-



Site

① Anti: septum

② Ant: wall [LV]

③ Lateral wall

④ Post-wall

⑤ RV MI

LAD

LAD

① circumflex

Post-Descenting

② marginal

Lead

V_2 (V_1 or V_3)

V_3, V_4 (V_2)

V_5, V_6, I, av_L

$V_7 - V_9 - ST \uparrow$
or

$V_1 - V_4 \rightarrow$ reciprocal
 $ST \downarrow$

RV_4

⑥ Inf wall

② coronary via post descending

$\text{II, III, aVF}_{104}$

⑦ Antero-Lateral MI

④ main coronary

$V_1 - V_6, I, aVL$

RxOC = CABG (not PCI)
↓
not feasible

⑧ Cardiac Markers

Time to ↑ in blood (after symptoms)

Time to ⑨

1) Heart Type FA Binding Protein

2 hrs

24 hrs

2) Myoglobin

3 hrs

24 hrs

3) Troponin I [Best]
T

6 hrs

10-14 days

4) CPK-MB

6 hrs

72 hrs

↳ Preferred over Troponin if re-infarct 3-10 days

Troponin can be used in re-infarct.

if >20% ↑ from previous.

Rx (I) ST ↑ MI

105

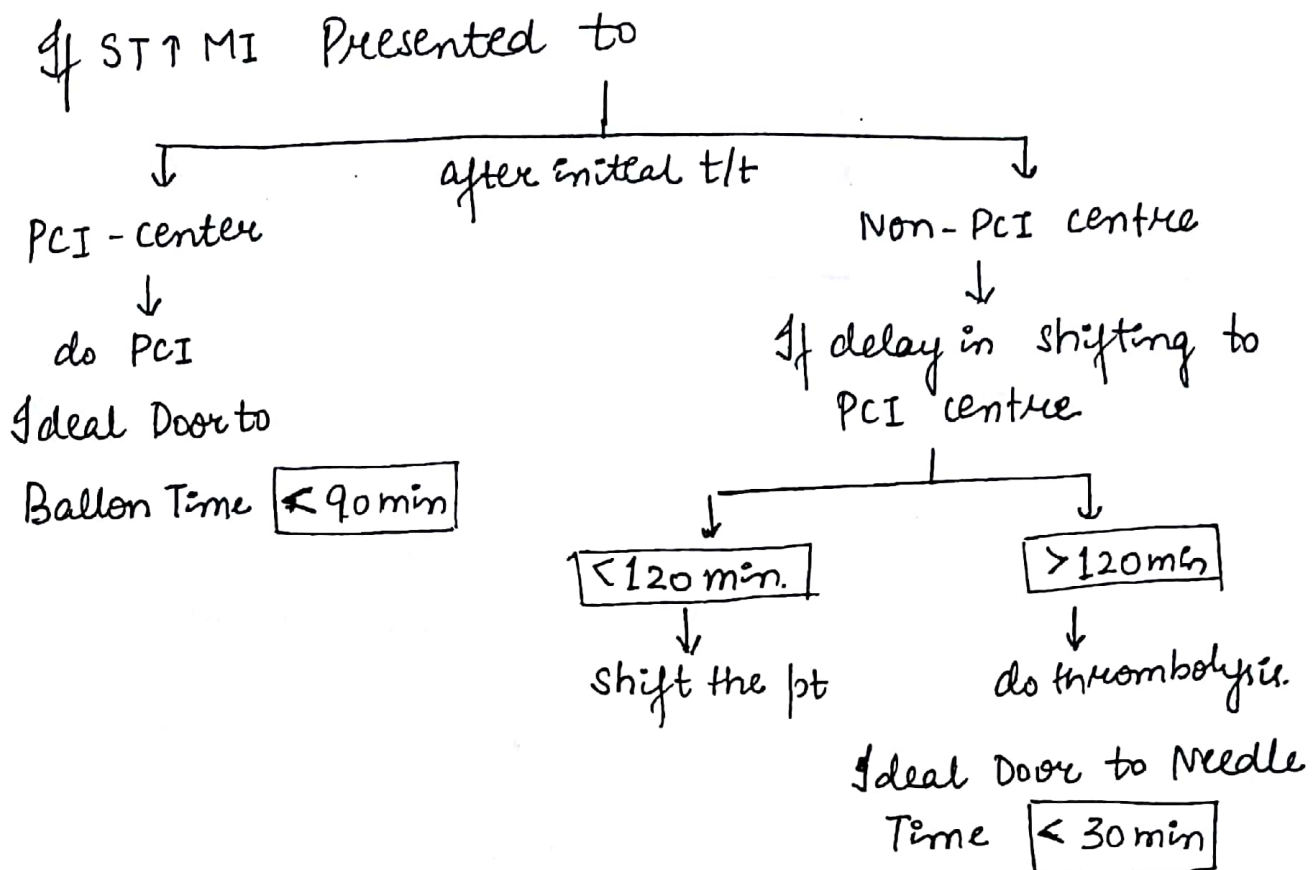
Initial Rx

Role

- 1> **Aspirin** [non-enteric coated] Essential in all
Dose - 325mg chewable
- 2> **O₂ inhalation** → if O₂ saturation is ↓
- 3> **I.V. Morphine** → Analgesic
+
Ac. cardiogenic Pulmonary edema
- 4> C/I in **RVMI**
[↓ preload → further ↓ CO]
- 4> **Nitrate** → coronary vasodilatation.
+
if BP ↑
- 5> C/I - **RVMI**
- 5> **β blocker**
metoprolol → ↓ workload
C/I - Asthma
PR interval > 0.25 sec
- 6> **ACEI** → All pts. for initial 48 hours
↓
Continue if HT (+)
- 7> **High Dose Statins** → Anti-inflammatory +
Atorva 80mg/d. Plaque stabilising Property.
- 8> **Clopidogrel** → if pt undergoing procedure
300mg loading Dose PCI.

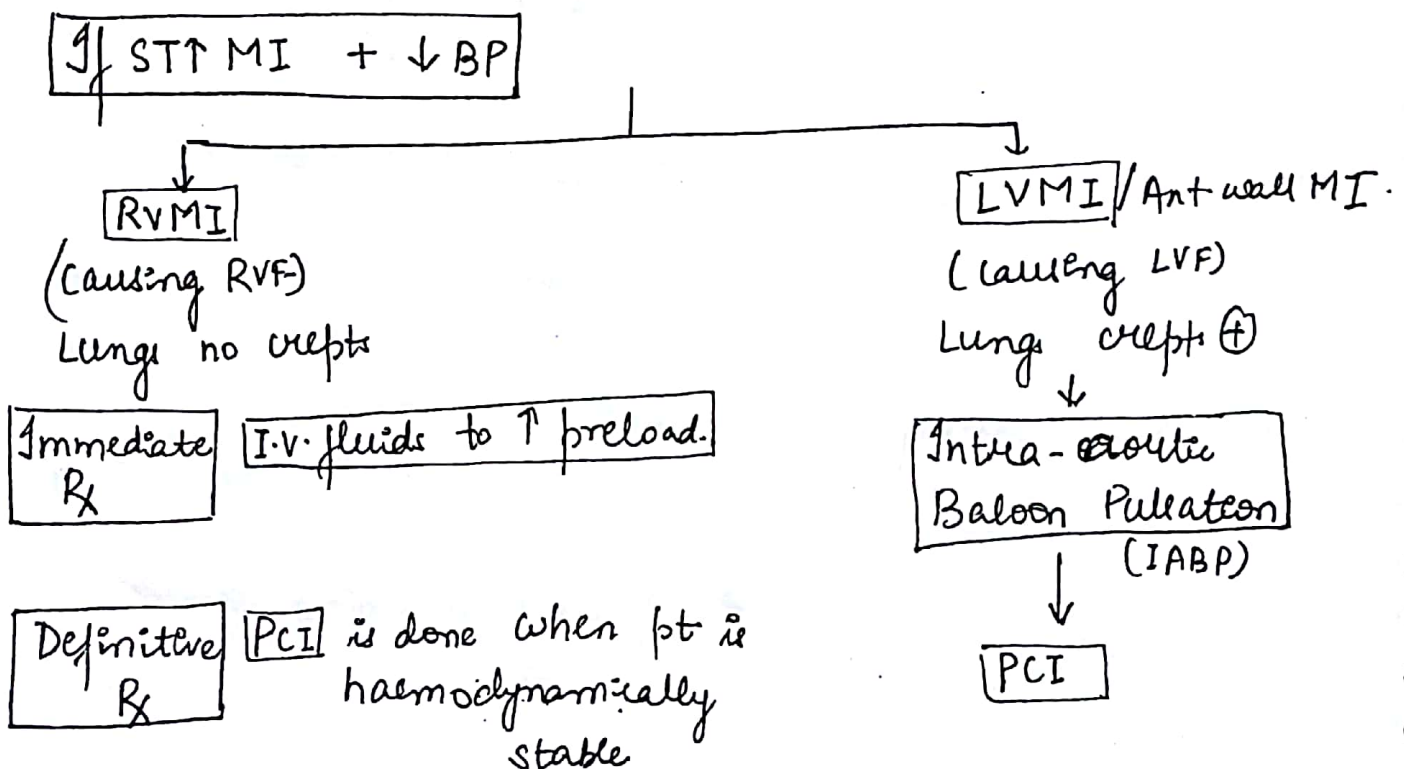
Definitive. $R_{OC} = \boxed{\text{PCI} > \text{Thrombolysis}}$

106



If symptom < 12 hours duration.

ST↑



Rx (II) Non-ST ↑ MI / Unstable Angina

107

Std. Rx

1) Anti-platelets = aspirin + clopidogrel

+

2) Anti-thrombotic agents = LMWH or Thrombin ⊖

+

③ Nitrate

+

④ β blocker

↓ if there is no relief

Add CCB

↓ if no relief

PCI

(III) Stable Angina

1) Aspirin Life long

2) Sublingual dinitrate

3) Rx risk factors

PRINZMETAL ANGINA

Cause - Idiopathic vasospasm of epicardial coronary artery. [non-atherosclerotic]

M/c artery affected → R Coronary

C/F -

• Smoker + young age

* Associated symptoms = Raynaud's phenomenon

* Pain = 12 AM to 8 AM.

I_x - ECG - ST ↑
Troponin = (N)

108

- R_x -
- 1) Acute → vasodilators = Nitrate → [CCB α-Blocker]
 - 2) Maintenance → (CCB)
 - 3)

C/I → Aspirin
β blocker

 → ⊖ / Lower vasodilator PGI
→ ppt. vasospasm

Q. In intraoperative MI ⊆ drug not used.

Ⓐ Heparin

Ⓑ Atropin if AVBlock

Ⓒ CCB

Ⓓ NTG.

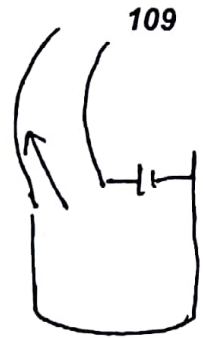
Best ECG Lead V₅ or V₄

LMP.

AORTIC DISSECTION

[causes -

1) M/c → HTN M/c site → ascending aorta (R)
Lateral wall



2) Large vessel vasculitis
Takayasu
Giant cell arteritis.

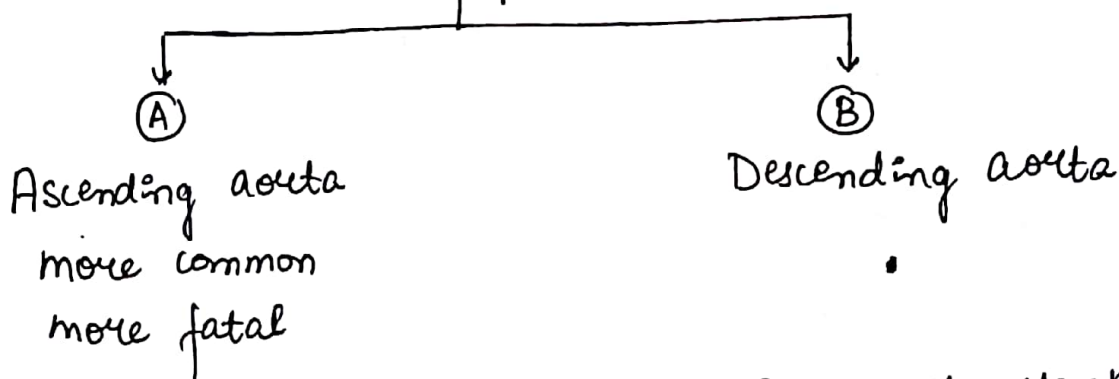
3) Atherosclerosis [M/c of aortic aneurysm]

4) Drug - cocaine

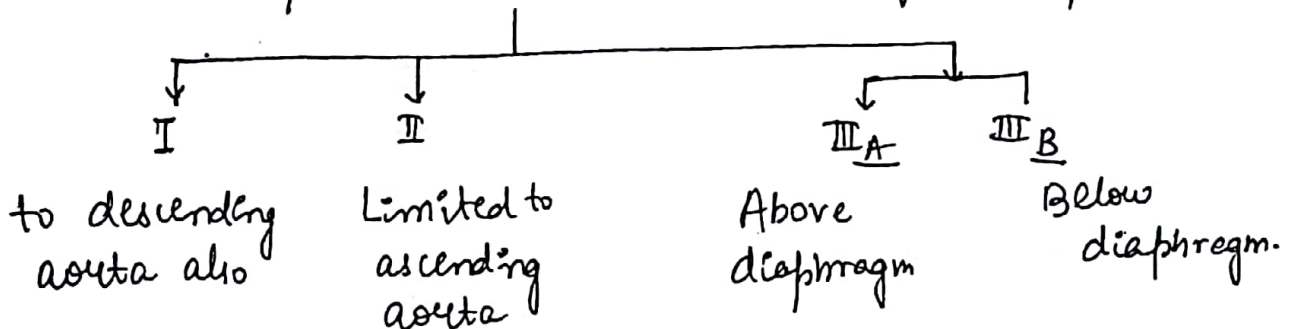
5) (C)
+

Types

A/c to site of Origin [Stanford classification]



A/c to extension [DeBakey classification]



Symptom

M/c - Chest pain

Retrosternal + 'Tearing' Pain + Radiation to¹¹⁰
interscapular
area

Sign

Asymmetrical Pulses

Acute Aortic Regurgitation. [due to type A dissecⁿ]

Ix

1) CXR → wide mediastinum

+
② Sided Pleural effusion (20%)

↓

D/D of Oesophageal Rupture

↓

H/o vomiting

2) Unstable pt. → Trans oesophageal ECHO.

3) If pt. is stable → CT

4) Gold Std. Ix → MR angio

R_x

Initial R_x → BP

High or (N) ————— Low

(Target SBP 100-120 mmHg)

I.v. ESMOLOL

I.v. fluids.

Definitive R_x

Type

111

A

Urgent Surgical
Repair.

B

Conservative

do surgery if

* Impending rupture

* Limb/visceral ischaemia

RHEUMATOLOGY

IMMUNE SYSTEM

115

INNATE

- 1> **ANATOMICAL BARRIER**
- 2> **PRR's** (Pattern Recognizing Receptors)
Inflammasome Proteins (SENSORS)
- 3> **Anti-Microbial Peptides (AMPs)**
Lysozymes - Tears/saliva

4> **NK cells (BOUNCERS)**

Largest WBC

Regulated by T cells (IL-2)
Immune + Tumour surveillance
Non-immune mediated action
Only Immune cell → non-MHC
restricted action.

(virus infected / mutated cells
are also checked by these cells)

5> **MONOCYTE - MACROPHAGE SYSTEM** (Police)

6> **Dendritic cells** (Most Potent APC's)

7> **GRANULOCYTE SERIES (N, B, E)**

8> **COMPLEMENT CASCADE.** Regulators of immune response

a) **CYTOKINE**

ADAPTIVE

1> **B cells (HUMORAL)**

- Express CD19, 20 on
surface

- when activated

↓
PLASMA CELLS

↓
Immunoglobulins
(antibodies)

2> **T cells (cell mediated)**

CD4 (Helper) CD8 (Cytotoxic)
Most Potent Level of
Immunity

IMMUNE EXCESS DISORDERS

116

INNATE (AUTOINFLAMMATORY)

FAMILIAL MEDITERRANEAN FEVER (FME)

(Recurrent Poly-Seratitis)*

EPID → 10-20yrs, ♂ & ♀

ETIOPATH → Inherited defect of
MEFV gene

Overexpression of the PRR's
INNATE EXCESS STATE

C/F → Recurrent Febrile Illness
(each last for 6-8 weeks)

Constitutional symp^s:- Anorexia
wt. loss
myalgia

HLI ↓			
Pleuritis	Peritonitis	Arthritides	Pericarditis
D/D - TB	D/D - Appendicitis	D/D - Juvenile RA	D/D - Rheumatic fever

A:- Clinical suspicion → GS (Genetic testing MEFV gene)

R_x:- COLCHICIN - Favourable response + longterm remission.

Dreaded complication :- 2° Amyloidosis - Nephrotic syndrome
High Mortality

Recurrent Febrile Illness = Unconfirmed Infection
= Rheumatology

ADAPTIVE

(AUTOIMMUNE DISORDER)

A) ORGAN SPECIFIC

Myasthenia Gravis

Grave's

Pernicious Anaemia

B) SYSTEMIC

= RHEUMATOLOGY

Study of systemic autoimmune disorders.

↓
ANTIBODY TESTING
INDEX

117

LUPUS group
(Skin rash)
"Wolf-Bite"

- 1) SLE
- 2) Systemic sclerosis
- 3) Sjogrens (sicca)
- 4) M.C.T.D.
- 5) Rheupus

ARTHRITIS
Approach.

- 1) RA
- 2) Spondylo
arthropathy
- 3) Crystal induced
- 4) CHARCOT'S joint
(neuropathic)

VASCULITIS

- 1) Misc. Pain syndrom
• fibromyalgia
- chronic fatigue
syndrome

ANTIBODY	CLINICAL SIGNIFICANCE (Best screening)	
ANA	M/c Ig found in autoimmune Disorders (>98% of case) MOST SENSITIVE Ig	
<u>ELISA</u> Qualitative Result (+/-) Hence it is non specific	METHODS → <u>IF</u> (Preferred) 1) Quantitative (Result in titres) $<1:160 = \oplus$ in 20% Healthy population $>1:160 = \text{SIGNIFICANT}$ (More specific) 2) IF PATTERN (due to the Δ)	
IF PATTERN <u>M/c</u> - SPECKLED	ANTIBODY Anti-Ro/La [SSA/SSB]	DIAGNOSIS Sicca SYNDROME.
Homogenous Rim pattern	Anti-dsDNA - M/c in SLE Anti-Smith - Most specific for SLE	} SLE
Centromere Nucleolar Pattern	Anti-centromere (specific) Anti-topoisomerase-1 (SCL-70 commercial)	→ Localised systemic sclerosis → Systemic sclerosis

ANTIBODY

CLINICAL SIGNIFICANCE

(Aste Role in SLE)

Anti-Sm
(not preferred)

Most SPECIFIC for SLE
Only in 10% (lacks sensitivity)
NO correlation \bar{c} disease activity

Anti-ds DNA
(preferred)

Ⓟ Sensitive & Specific
correlates \bar{c} disease severity
Associated \bar{c} \uparrow Risk - nephritis/CNS involve-
ment

APLA
(phospholipid)

Present in 60-70% cases of SLE
Associated \bar{c} vascular thrombosis (fetal Loss)
Most recent to be ~~in~~ included in
 Δ criteria of SLE.

Anti-Histone
(specific for
Drug induced
SLE)

CVS ^{HIC} ACEI, β blockers, Thiazides, Statins
Methyldopa, Hydralazine, Procainamide

Anti-microbial INH, Dapsone, Sulfonamides

CNS Phenytoin, carbamazepine

GIT ~~Sulfono~~ Sulfasalazine,

Endo Propylthiouracil

Misc d-penicillamine

New Interferons
Anti-TNF α

ANTIBODY	CLINICAL SIGNIFICANCE. (Prognostic Role)	
Anti (Ro/La) ↓ crosses placenta	↑ Risk of Congenital Lupus ↓ Risk of maternal Nephritis	SSA/SSB ¹²⁰ Asteric Role in SCLL A Syndrome
Anti-Ribosomal P	↑ Neuro-psychiatric convulsion + Psychosis	↑ Risk of CNS Lupus
Anti-Neuronal Ab	↑ Neuropathy R. Painful, AXONAL	
Anti-erythrocyte	Hemolytic anaemia	↑ Risk of hematological involvement
Anti-platelet	Thrombocytopenia	

ANTIBODY	CLINICAL SIGNIFICANCE	
Anti-centromere	Localised Scleroderma (CREST syndrome)	Asteric Role in SSC
Anti-SCL70	Diffuse SSC	
Anti-U ₃ RNP	↑ Risk of PAH + RPAH	Prognostic Role in SSC.
Anti-U1RNP	Specific for Mixed Connective Tissue Disorder	
Rheumatoid factor (RAF) IgM Ig against Fc portion of IgG	Best screening Test for RA (PROG) (SENSITIVE) Correlates - Risk Bone erosions (PROGNOSIS) Non-specific for Δ	

ACPA/Anti-CCP (Most specific for R.A.)	Anti-cyclic citrullinated protein Ab. (Aster Role in RA) 121	
ANCA (Anti-neutrophil cytoplasmic Ag)	Vasculitis (Aster Role)	
	CANCA Anti-PR3 (proteinase-3)	pANCA Anti-MPO (myeloperoxidase)

SLE

M/c autoimmune disorder

Epid- 20,40 yrs. $\text{♀} > \text{♂}$

Cause- Idiopathic M/c

Risk factors -

- 1> GENETIC - TREX-1 gene defect
- 2> CHROMOSOMAL - Klinefelter's syn.
- 3> INFECTIONS - EBV
- 4> TOXINS - UV Rays, Silica

Manifestation	Clinical Description.
1> Cutaneous	<ul style="list-style-type: none"> a> Acute :- MALAR RASH b> Chronic :- DISCOID RASH
2> Oral ulcers (considered as SLE)	<ul style="list-style-type: none"> excluding - a) nutritional b) Infective c) Behcet's disease
3> alopecia (considered as SLE)	<ul style="list-style-type: none"> excluding - a) Nutritional (Iron, Zn) b) Endocrine - thyroiditis (Hypo) c) Drug induced
4> Synovitis (90%) (Nonerosive arthritis)	<p>(M/c) <u>Symmetrical polyarthritis</u></p> <p>NEVER DEFORMITY/ Bone Disease</p>

5) RENAL	Proteinuria > 3+, CManuloe/ RBC Cast
6) CNS	Neuropsych., neuropathy
7) ANAEMIA	Hemolytic - Hb \leq 10g/dL
8) LEUCOPENIA	WBC \leq 4000 or Lympho \leq 1000
9) Thrombocyto penia	Platelet \leq 1,00,000

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Δ :- SLICC Criteria (Systemic Lupus International Collaborative Clinics)

9 clinical	6 Immunological.	≥ 4 confirms SLE (atleast 1 of each)
ABOVE manifestations	1) ANCA ② Antism 3) Anti Ds DNA	④ APLA ⑤ Direct Coombs Test +ve ⑥ Low serum C ₃ Level

R_x

ACUTE SLE FLARE



Life-threatening features / causes of
ACUTE MORTALITY IN SLE

- 1) Lupus Nephritis (Type 3,4)
- 2) Neuropsychiatric manifestations
- 3) Coagulopathy / Pancytopenia

⊕

Autoimmune
Crisis

⊖

MILD FLARE



R_x . IV Methyl Prednisolone **PULSE** \Rightarrow Oral Prednisolone
1gm/day = 3-5 days

1-2mg/Kg/day

Add steroid sparing
MYCOPHENOLATE MOFETI

(Lifelong)

Approved alternatives to methylprednisolone

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RITUXIMAB (MAb \ominus CD₂₀)

BELIMUMAB (MAb \ominus BAF)

POOR ~~persons~~ PROGNOSIS

Affects Productive age group	unpredictable course of the disease	High cost of therapy	Long Term Adverse drug Rxn of immune suppression	NO CURE (lifelong therapy)
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ACUTE

← MORTALITY IN SLE

↓
CHRONIC/ Longterm

- 1) Thrombotic events - cardiac failure
- 2) Opportunistic Disease

SCLERODERMA → SYSTEMIC SCLEROSIS ¹²⁴

sclerosis | skin ⊗ >98% have systemic involvement.

Epid - 30-50yr, ♀ > ♂

Cause - H/c - Idiopathic

Risk factors → 1) INFECTION → CMV, Parvovirus B19

2) TOXIN EXPOSURE - Silica, Toxic oil syndrome

C/F ← H/c

1) RAYNAUD'S → can precede skin changes > 10 yrs



2) SKIN changes : Hands & face

	HANDS	FACE
a) OEDAMATOUS	Puffiness of fingers	& Face
b) INDURATIVE	claw hand deformity	Mask-like
c) SCLEROSIS (most specific) (MOST SPECIFIC)	Autoresorp ⁿ of terminal phalanx ↓ shortening of Digits	"FISH-MOUTH" appearance

CLASSIFICATION - Based on Extent of Skin Involvement

ONLY SKIN (<2% cases) MORPHIA [En-coup-de-sabre Lesion]	Restricted to face Distal to elbow ↓ Localised	Proximal - elbow Trunk ⊕ ↓ Diffuse	only organ. SCLERODERMA SINE SYNDROME (Least common)
sickle	SSC		

Suspected →

SSc

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Face & Distal to elbow
LOCALISED SSc

Proximal to elbow
DIFFUSE SSc

Anti-Centromere ⊕

SCL-70 / Topoisomerase - 1 Ab ⊕

Also called 'CREST'

✓ Calcinosis

✓ Raynaud's (Doc = CCB)

✓ Eso. dysmotility (GERD)

✓ Telangiectasia
s → sclerodactyly

Above features are M/C E
localised >> Diffuse

More risk of organ involvement

Lung: M/C type of ILD in autoimmune disorder

NSIP (non-specific interstitial)
↳ Doc = steroids pneumonia

• Iso. Pulmonary artery HTN
(Doc - iloprost)

• RPGN
(Renal vici) (Doc - captopril)

Rx = ONLY PALLIATIVE

NO CURE

Unfavourable Prognosis

SICCA SYNDROME

(Sjogren's Syndrome)

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M/c manifestation → Dryness of eyes & Mouth.

Lymphocytic infiltration of exocrine glands

CAUSES

1° SICCA (Idiopathic) (Rare)

[SICCA - is the Disease]

- High Risk → systemic (extraglandular manifestations)
- High titres → SSA/SSB Ab
- High Risk → LYMPHOMA (M/c of death in SICCA)
- Majority → Immunosuppressants.
- POOR PROGNOSIS

(M/c) 2° SICCA

[Underlying disease]

- SLE, SSC, MCTD, RA, vasculitis
- 1° Biliary Cirrhosis
- chr. autoimmune Hepatitis
- only Glandular symptoms
- Low titres - SSA/SSB
- NO risk of Lymphoma
- Rx - only palliative FAVOURABLE PROGNOSIS

C/R

GLANDULAR.

SYSTEMIC

Involved	C/R	TEST	Rx
Lacrimal Gland	Dry-eye	Schirmer	Artificial tears
	corneal or conjunctival erosions	Rose Bengal Test	Protective glasses
Salivary	Dry-mouth	Iontophoresis	Hydration
Pancreas	Maleb ⁿ Syndrome	Stool FAT estimation	enzyme replacement

[LUNGS] - M/c - NSIP

Isolated PAH

[Renal] - (M/c).

↳ Distal RTA.

- Interstitial nephritis

[Liver] - Cirrhosis

[CNS] - neuropathy

LYMPHOMA - most dreaded

Rx 2° sicca → only palliative
 1° sicca → Depends on organ involvement
GOOD PROGNOSIS (majority are 2°)

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POOR PROGNOSTIC FACTORS

- 1> Elderly onset (>40). ♀
- 2> B/L parotid enlarged
- 3> systemic ⊕
- 4> High titres of SSA/SSB.

OVERLAP SYNDROMES

Epid = 10-20 yrs, ♀ > ♂

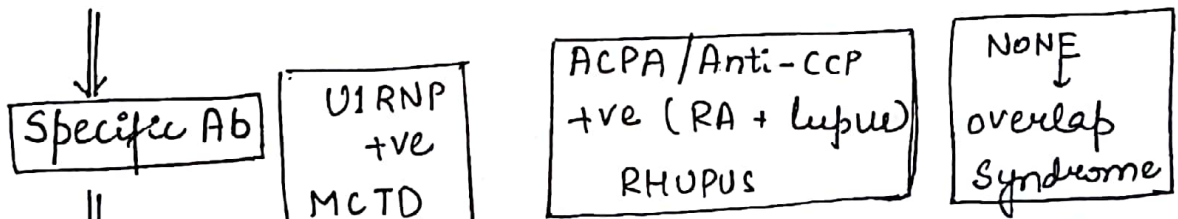
C/F = (SLE/SSC/sicca) + (R.A.)

Screening =

Ab

ANA
+ve

RF
+ve



Rx

SLE Dominant	RA Dominant
Immunosuppression	DMARDS
Non-erosive arthritis	Erosive arthritis

PROGNOSIS - Better than individual diseases
 Better response to therapy

APPROACH TO JOINT DISORDERS

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TRUE ARTICULAR	PAIN	PERT-ARTICULAR
✓	Active	✓
✓	Passive Movement	✗
INFLAMMATORY	MORNING STIFFNESS	DEGENERATIVE
>30 mins	DURATION	<30 mins
Resolves	AFTER ACTIVITY	WORSENS
		OSTEOARTHRITIS

APPROACH TO INFLAMMATORY ARTHRITIS

MONO (1 joint)	OLIGO (2-4 jts)	POLYARTHRITIS (≥5 jts)	
→ M/E Trauma → Septic GOUT	PSEUDOGOUT ↑ Crystal	AXIAL Ankylosing Spondylitis	APPENDICULAR - dominant
Symmetrical (small)		Asymmetrical (Large)	
RHEUMATOID ARTHRITIS	PSORIATIC ARTHROPATHY (Early DIP +)	ENTEROPATHIC ARTHROPATHY	REACTIVE ARTHRITIS
			Predominantly wt. bearing jt.
Spondyloarthropathy → ④ = AS + above 3			

M/c Pattern of Joint Involvement in Diseases

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Most Imp parameter for Diagnosis of arthritis

RHEUMATOID ARTHRITIS

Epid- 30,50yrs, ♀ > ♂

M/c - Idiopathic

Risk Factors - 1) GENETIC - HLA-DR4 (Most cases = sporadic)
2) INFECTION = Mycoplasma, EBV

C/F

ARTICULAR (predominant)

EXTRA-ARTICULAR

- Inflammatory Poly-arthritis
- Appendicular Dominant
- Spine involvement - rare
↳ M/c - Atlanto-axial jt.
- Symmetrical, small jts of hand
Wrist, MCP jt, PIP jt

EPISCLERITIS

LUNG M/c Usual Interstitial
Pneumonia (UIP)

M/c → ♂

Pericarditis
Valvular M/c → MR

MUSCULO-SKELETAL
↓
Myopathy Osteopenia
Fast progress - OA

FELTY'S (RA + spleen)

↓
Anaemia / Neutropenia
Risk of Lymphoma
Least common
≤ 1% - advanced RA
Early DMARD Rx

NORMAL

[Articular str.]

SYNOVIAL
MEMBRANE

CARTILAGE
END PLATE

BONE



STAGE-RA

1) SYNOVITIS

2) PANNUS
FORMATION

3) BONE EROSION

↓
Jt. Destructⁿ

Jt. Deformity

(irreversible stage
of Disease)

Δ :- EULAR (European League against Rheumatism)
Guidelines - A scoring system ¹³⁰

Ⓐ PATTERN of joint involvement (Max : 5)

- 1 jt (Predom. Large) → 0
- 2 - 10 jt → 1
- 1 - 3 jts → 2
- 4 - 10 jts (Predom. Small) → 3
- > 10 jts → 5

Ⓑ SEROLOGY (Both RF & ACPA) [Max = 3]

NEGATIVE → 0

MILD ⊕ [$< 3 \times$ upper normal limit] → 2

STRONG ⊕ [$> 3 \times$ upper limit] → 3

Ⓒ DURATION

< 6 wks - 0
> 6 wks - 1

Ⓓ ACUTE PHASE REACTANT

NEGATIVE → 0

ELEVATED → 1

Δ = ≥ 6 confirms RA.

RADIOLOGY (X) → NOT recommended for Ase.

OLD CRITERIA:- X-Ray Hand	Bone Erosions
<p>X-Ray - Least sensitive test</p> <p>MRI - MOST SENSITIVE test</p> <p>↓</p> <p>Impractical</p>	<p>131</p> <p>↓</p> <p>Late, irreversible stage</p> <p>Earliest feature of RA</p> <p>Juxta-articular osteopenia</p> <p>↓</p> <p>NON-SPECIFIC.</p>

Rx Most preferred method → STAGE the severity
CDAI (Clinical Disease Activity Index)

2-8 - 10	10-22	>22
MILD RA	MODERATE RA	SEVERE RA
Single DMARD	COMBINATION DMARD	Early use of Biologicals

Prognosis:- Favourable → **REMISSION** → can be achieved in 60-85% cases

POOR PROGNOSTIC FACTORS :-

- 1> Elderly (>40)
- 2> ♀
- 3> >10 jts @ onset
- 4> High titres of RF
- 5> Delay in initiation of DMARD ≥ 3 months

DMARDS	Ind ⁿ	ADR	Follow-up ¹³²
METHOTREXATE (MTX)	1st choice (B) single or combination.	BM ↓, Hepatotoxicity (Dose dependent S/E)	CBC, LFT - 3 monthly
	Back bone of Biologics	MTX induced ILD unpredictable Permanent C/I to MTX use	CXR, PFT Baseline & Annually
		Teratogenicity	Counseling
HYDROXY- CHLOROQUINE	Safest in (B) 2 nd choice	Bull's maculo pathy (Irreversible)	Fundus, Exam ⁿ , Perimetry Baseline & annually SOS
SULFASALAZINE	Safe in (B) 3 rd choice	Gastritis Hepatotoxicity	LFT - Baseline & 3 monthly
LEFLUNOMIDE	Approved as Mono Rx Completed Family MODEST efficacy (limited use)	No synergy w/ other DMARDS 6X ↑ Hepatotoxicity Teratogenicity	Stop ≥ 2 ovulatory cycles before conception.

BIOLOGICALS = Pathophysiology of R.A.

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↑↑↑ Pro-inflammatory Cytokines

TNFα most potent + **IL-1**
(MOST PREFERRED)
Anti-TNFα agents
ANAKINRA

IL-6
TOCILIZUMAB

Stimulates T cell
MODULATOR = ABATERCEPT

Stimulates B cell
RITUXIMAB

Intracellular signalling pathways of Inflammation

eg. ~~JAK~~ JAK - Janus associated Kinase

TOFACITINIB - Tyrosine Kinase \ominus of JAK. - 1st oral Biological

ANTI - TNF α AGENTS ADALIMUMAB, GOLIMUMAB
S/C every 2-3wk

~~ETARER~~
ETARNACEPT

INFLIXIMAB

PEGYLATED CERTOLIZUMAB

Chimeric form
Mab against
TNF α receptor

Chimeric Mab
against
TNFα itself

Fully Humanised Mab
against
TNFα. itself

S/C every
6-8 weeks

Limited
efficacy

Excellent
efficacy
Anaphylaxis

Equal efficacy
safety

Common

Common ADR \Rightarrow Reactivation of TB.

Hence, screening for active/dormant TB is mandatory before Anti-TNF α agents.

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Tuberculin (MANTOUX) \rightarrow MOST SENSITIVE. \rightarrow BCG vaccination. (false +ve)	WHO \rightarrow In countries (BCG vac.) Best screening Test is Interferon γ assay (TB-GOLD/quantiferon) quantiferon
--	--

SPONDYLOARTHROPATHY

Group of Disorders characterised by

COMMON FEATURES

- 1) Seronegative RAF -ve
- 2) HLA B27 +ve Strong family History
- 3) 1^o Site - "Entesis" Juncⁿ Btw Bone & Tendon.
- 4) Axial Involvement is not Uncommon.
- 5) Extraarticular manifestations predominate
- 6) Excellent response to NSAIDs \rightarrow 1st Line of Rx

SpA are D/D - Inflammatory Polyarthritides

I ANKYLOSING SPON. / BECHETROW'S / MARIE-STRUMPELL DISEASE 35

Epid - 10-20yrs, $\sigma > \eta$, 90% - HLA B27

C/F ARTICULAR
(Axial Dominant)

Sacro-iliac Joint - H/C	LBP (non-specific) always B/L But asymmetrical
Lumbar spine	Restricted resp. movement toward bending
Thoracic spine	Restricted resp. movement
Cervical spine	Highest risk of # in lower part of Cx spine

EXTR-ARTICULAR
(Predominant)

70% → Recurrent u/L ANT. UVEITIS

A

BEFORE

Spine Involvement

AFTER

HLA-B27 → (+ve)
↓
≥ 2 common features of SpA
(confirms A.S.)
(-ve) (X)

MRI proven sacroileitis
↓
≥ 1 common features of SpA

NORMAL	STAGES	Rx
vertebral Body	ENTHESIS	NSAIDS 136
Tendon of Paraspinal Muscles	MARROW EDEMA	BEST TIME for Biologically.
	MARGINAL SYN DESMOPHYTES (unique feature)	DMARDS Biologicals (All TNF α agents)
	FUSION (ANKYLOSIS)	

MRI is mandatory

Only Test → Detect the stage of A.S.

R_x - UNFAVOURABLE

unlike RA only 10-15% active complete Remission

II PSORIATIC	III ENTEROPATHIC	IV REACTIVE
M/c - "Gutlate" / Pustular type of psoriasis	M/c - U.C. / Crohn's Disease	Post-infective
	Common Pathology	F./UTI CHLAMYDIA
	Bowel Disease & Severity of activity arthritis	URBAN S. Typhi
		Travel Diarrhoea Shigella
M/c - 'ONCHOLYSIS' (nail pitting) Skin Lesions 10% uveitis ant ↓ Symmetrical poly-arthritis (Predom - small jts) mimic RA - 5-10% pts arthritis > skin changes	M/c - Diarrhoea Most-specific = Pyoderma gangrenosum (Unique in U.C.) ↓ Asymmetrical poly arthritis (Predom - Large jts)	M/c → Febrile illness KERATODERMA BLENORRHOAGIA (Keratotic, Painless plaques - soles + Palm) ↓ Asymmetrical - polyarth (Predom - wt-bearing jts)

Early DIP jt ⊕
x-Ray → pencil in cup deformity

• MTx

• Anti-TNF agents

• Tofacitinib

Sulfasalazine
Anti-TNF

Hydroxychloroquine
(additional anti-inflammatory action)

CRYSTAL INDUCED

GOUT

PSEUDOGOUT

Crystal	Mon. sodium urate (M.S.U.)	Ca^{2+} pyrophos. dihydrate (C.P.P.D)
Epid	30-50 yrs $\sigma > \phi$	>50 yrs $\sigma > \phi$
Etiopath	90% - Renal Defect in urate excretion. 10% - Diet/Drugs (Pyriznamide/thiazide)	90% - Jt. Degeneration. <div>10% - Hypercalcaemia = severe PTH adenoma so, early Paraneoplastic syn</div>
C/F	Acute - Inflammatory MONO- ARTHRITIS (M/c - 1st MTP, ankle jt)	Acute, inflammatory OLIGO (M/c - Knee, Hips, shoulder)
Swelling	Serum Uric Acid	NON-SPECIFIC NORMAL VALUE DOESN'T exclude S. Ca^{2+}
Synovial Fluid Analysis	NEEDLE SHAPED	RHOMBOID SHAPED
Polarising microscopy	STRONG -ve Birefringence	MILD +ve Birefringence
Demonstrate crystals	Gold Std.	

Rx

Acute Attack

Colchicine

Canakinumab

MAB

IL-1 β

NSAIDS

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Renal Failure

FEBUXOSTAT (X-O-I)

Hepatic excretion.

Additional anti-inflammatory

Intra-articular Steroids

Chronic

Prevention

TARGET Uric acid < 6mg/dL

1st Line: X-O-Inhibitors

(Allopurinol, Febuxostat)

Encourage Physiotherapy

Avoid unnecessary

Ca²⁺/vit D₃ supplements

In elderly

Majority require

Jt. Replacement Sx.

Refractory cases

PEGLOTICASE

Regulated uricase

debulking action on tubules

Prog

Favourable

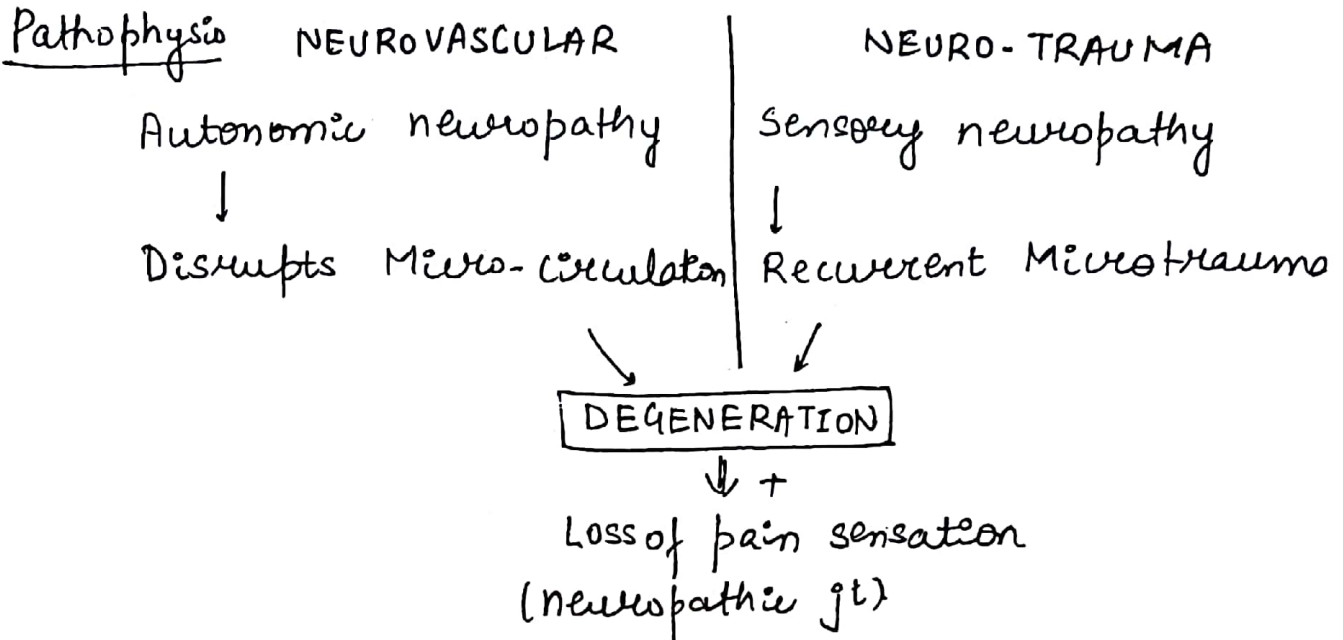
Unfavourable

CHARCOT'S

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1st described - Tabes (Neurosyphilis)

Associations :- M/C DM, Leprosy, Amyloidosis



M/C Forefoot Jt → Hind foot Jt → Ankle Jt

Ass XR → 'Loose Bodies' in jt. cavity

Only Rx Strict Immobilisation → Total Rest

↓
facilitate recovery of
Jt.

only palliative → Unfavourable Prog.

VASCULITIS

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① Based - Pathological Mechanisms

ANTIBODY (ANCA) MEDIATED	IMMUNE-complex MEDIATED	T. cell mediated
Wegener's (W.G.) Churg Strauss (C.S.S.) M.P.A. Microscopic polyangitis	Hep. B - PAN Hep C - Cryoglob H.S.P. (Henoch-Schönlein Purpura)	Giant cell arteritis Takayasu's W.G. C.S.S.

② Based - size of vessel affected (Preferred)

LARGE	MEDIUM	SMALL
Giant cell arteritis Takayasu	Polyarteritis nodosa Kawasaki	
ANCA +ve		ANCA -ve
Anti-PR3 W.G.	Anti-MPO M.P.A. C.S.S.	H.S.P. vs Hypersensitivity Cryoglobulinemia BECHET'S Disease

> 50 yrs, ♀ > ♂

C/F - Artery Involved (Carotid)		PATHOLOGY
Br. of EXTERNAL CAROTID	Br. of INT. CAROTID	Polymyalgia Rheumatica
H/c - <u>Sub-Temporal</u> Headache (wave-supine) ± Diplopia ± Jaw claudication Pain ± Paraesthesia over Jaw	1st Br. Ophthalmic A. End artery - No collaterals. ↓ Permanent BLINDNESS	

ESR (screening) > 60 (significant)

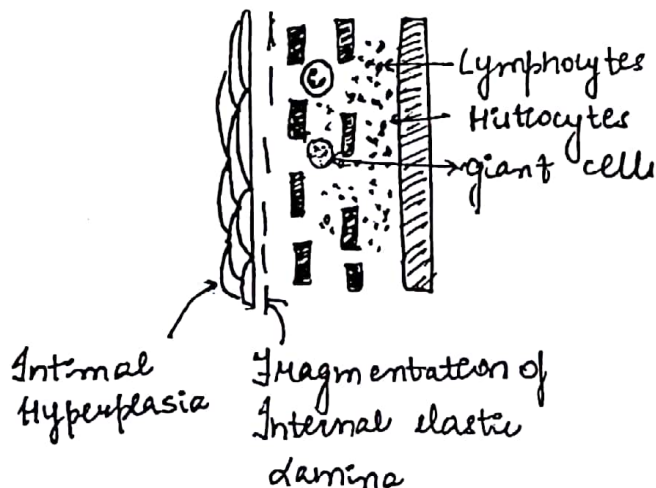
Gold Std →

↳ Temporal A. Biopsy → Minimum > 2cm Length.
 → HPE - Granulomatous vasculitis

R_x = Steroids → Relief of symptoms

↳ only drug to prevent dreaded complication
 = BLINDNESS

Early R_x = GOOD R PROGNOSIS



TAKAYASUS / AORTIC ARCH SYNDROME

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Epid- 10-20yrs $\sigma > \sigma$

c/f- Depends on artery Involved = All direct Br. of AORTA

SUBCLAVIAN (H/C)	CAROTID VERTEBRAL	COELIAC	RENAL	CORONARY <1%
U/L claudication	Recurrent	Chr. mesenteric	Refractory HTN	Acute Coronary Syndrome
Unequal/ABSENT PULSELESS DISEASE	TIA/Stroke	Insufficiency	(RAS)	

Δ - CT- AORTOGRAPHY Gold Std

Rx- Immunosuppression + Angioplasty
(Specific) (Palliation)

POOR PROGNOSIS

KAWASAKI'S / Mucocutaneous L.N. Syndrome

H/c vasculitis ; <5yrs, $\sigma > \sigma$

Replaced R.H.D. \rightarrow M/c cause of cardiac death in children. due to Acquired heart Disease

AHA Guidelines

H/c manifestation \rightarrow Febrile episode

Any Fever - on/after 4th Day (min. dur 5 days)⁹⁰

If - 4/5 of following features are (+)

- 1) 90% B/L non-exudative conjunctivitis
- 2) Erythema over extremities
- 3) Peri-anal Rash
- 4) Strawberry Tongue
- 5) non-suppurative single, cervical L.N.

~~Rx~~ - IVIg + Longterm Aspirin prophylaxis

- Relieve symptoms
- Reduces risk of coronary involvement to 4-6%
- cannot reverse coronary aneurysm

Dreaded : CORONARY ANEURYSM complication

RUPTURE
(4-6% case)

THROMBOSIS
95% of cases

↓
elective angioplasty prevents.

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Prognosis - **FAVOURABLE**

ULINASTATIN :- Neutrophil elastase Inhibitor.
(New, approved) only IVIg refractory case.

PAN / SYSTEMIC
NECROTISING
VASCULITIS

MPA (part of PAN prior to 1999)

Epid 30-50 yrs. ♂ > ♀

Etiology Classical H/C - Idiopathic

30% Chx. Hep B infection

Pathology Immune complex
Mediated
↓ Fibrinoid necrosis
Bifurcation of Medium vessel
↓
Microaneurysm formation

ANCA-mediated vasculitis
↓
small vessel predominant
↓
70% Anti-MPO +ve.

C/F H/C 90% arthralgia

HEMATURIA - **CO out GN**
(rupture of micro aneurysm)

always due to GN

CNS- Mononeuritis + multiplex (neuropathy) - asymmetrical

SKIN- Raynaud's phenomenon

Digital gangrene, LIVEDO		Purpuric Rash
Coronadal arteries mimic torsion	Pulmonary Spaceed But bronchial may be involved	Alveolar H ^{ge} (ANCA +ve → D/D - Good Pasture's Syndrome)

Δsis - Exception

Biopsy - Gold std

Renal angio-
mura aneurysm @
Bifurcation of vessels.

R_x Immunosuppressants → Favourable Prognosis

WEGENER'S GRANULOMATOSIS.

or Chronic Granulomatous angitis

30-50 yrs, ♂ > ♀

Closest D/D → Good Pasture's .

C/F	Pulmonary	Renal	Eyes
H/c ↓ Lungs	URT ^a specific H/c - chr. sinusitis	RPGN	H/c - Pan-uveitis
• B/L abscess	• Nasal bridge deformity		SKIN
• Multiple thin walled cavity	• Serous otitis media (GLUE)		Purpuric Rash over L.L.
• Alveolar H ^{ge}	• Subglottic stenosis (change in timbre of voice)		

Serology 70% Anti PR3 +ve (Wegener's Antigen)
 (SCREENING) 30% Anti MPO +ve
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 Anti: Absence cannot exclude W.G.

BEST TEST → LUNG BIOPSY

Rx cyclophosphamide → favourable response
 GOOD & PROGNOSIS

~~CH~~
 CHURCH STRAUSS (eosinophilia & granulomatous
 angitis)

30-50 yrs. ♂ > ♀

C/F	PULMONARY	RENAL	SKIN involvement
LUNG Late onset asthma	URT allergic rhinitis	↓ RPGN	Purpuric/ urticarial rash

W.G. can be differentiated by ocular involvement

Asx- ~~short course of steroids~~

Lung Biopsy / skin Bx = eosinophilic
vasculitis

Rx- short course of steroids
 favourable prognosis, Long term remission.
 GOOD & PROGNOSIS

H.S.P. (ANAPHYLACTOID PURPURA)

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>90% cases - occurs <10yrs age M > F.

ADULT H.S.P.

HYPERSENSITIVITY
VASCULITIS

EPID - 20-40yrs, M > F

Etiopath Post Infective H/C - preceded by URTI

C/F	PALPABLE PURPURA	
LL + Buttocks	Distribution	Generalised
Common Abd. pain, Melaena	Mucous memb. involvement	Uncommon
3-5% - IgA deposits on GBM - Gross Hematuria	Renal involve- ment	NEVER occurs
Capillaries	Site - Biopsy (Gold std)	Post capillary venule

Rx - Reassurance / Self Limiting Disease.

ESSENTIAL MIXED CRYOGLOBULINEMIA (EMC) 147

↓
usually indicate
Idiopathic cause

Majority = 90% = 2^o cause

✓ Multiple myeloma

✓ chr. Hep. C, Hep B

✓ Lymphoproliferative states

Pathophy:- Exposure to cold → Cryoglobulins ppt
($T < 37^{\circ}\text{C}$) (Ig \leq ppt.)

↓
H/c - Skin capillaries
98% - multiple areas of skin
neurosis

↓
Renal tubulus
A.T.N. (Direct toxicity)

Δ su. Incubate plasma in cold bath → ppt. ⊕

Rx + Prog - underlying cause (unfavourable)

BEHCHET'S DISEASE → HLA B5¹₁₄₈

epid- 30-50 yrs, ♀ > ♂ (worse in ♂)

MAJOR

Recurrent, painful,
oral aphthous
ulcers

MINOR

- 1> Recurrent superficial thrombophlebitis
- 2> B/L Hypopyon
- 3> Erythema ~~in~~ nodosum
- 4> Painful genital ulcers
- 5> Pathergy Test +ve
Skin Prick > 5mm deep

↓
Induration (+)

Δs - MAJOR + 2 MINOR - confirms.

R_x - Steroids - excellent response
Favourable Prognosis

FIBROMYALGIA (Pain Sensitivity Syndrome)

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Epid - 30-50yr, ♀ > ♂

Risk - stress

Pathophys - ↓↓ Blood flow to Hypothalamus
(MINOR) ↓↓ Cortisol response to stress

C/F - Multiple aches & pains (Somatic complaint)
≥ 3 months

• Associated c Defect of NREM sleep

Ass - Clinical - 18 point pain testing (screening)
(> 11/18 +ve tenderness → significant)

MR spectroscopy - gold std.

R_x - Pregabalin.
Gabapentin
TCA
SSRI.

Unfavourable Prognosis → Prone to analgesic abuse
Poor Q.L.I.

CHRONIC FATIGUE SYNDROME

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20-40yrs, ♂ > ♀

e/f - FATIGUE > 6 weeks

Asu - of exclusion

1> Obesity

2> Substance abuse

3> All medical causes

→ Nutritional

→ 2) Endocrine

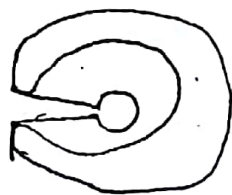
Hypothy, DM.

→ 3) Chx. Infection

→ 4) autoimmune

→ 5) neoplasm

Rx = Lifestyle Modification



RESPIRATORY

LUNG DEVELOPMENT

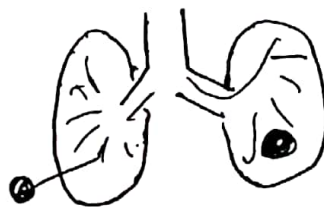
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5 stages

- 1) Embryonic stage → Lung buds
- 2) Pseudoglandular Stage - upto terminal Bronchiole
- 3) Canicular - Alveolar ducts
- 4) Sacular - Primitive alveoli
- 5) Alveolar - Mature alveoli

BRONCHOPULMONARY SEQUESTRATION

Defⁿ: Separation of part of lung during development from tracheobronchial tree & separate blood supply



TYPES

EXTRA LOBAR

Separated & having separate covering

INTRALOBAR

Separated part in adjacent lung of ~~not~~ covered by lung's pleura

M/c site → (L) lower lobe post basal segment

M/c Blood → Thoracic aorta supply

IOC :- CT Angiography or MR angiography

Rx - Resection if pt. is symptomatic

SURFACTANT

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- 1) Dipalmitoyl Phosphatidyl choline / Lecithin.
- 2) Produced by Type II pneumocytes
- 3) also by Clara cells.
- 4) Removed by Alveolar macrophage

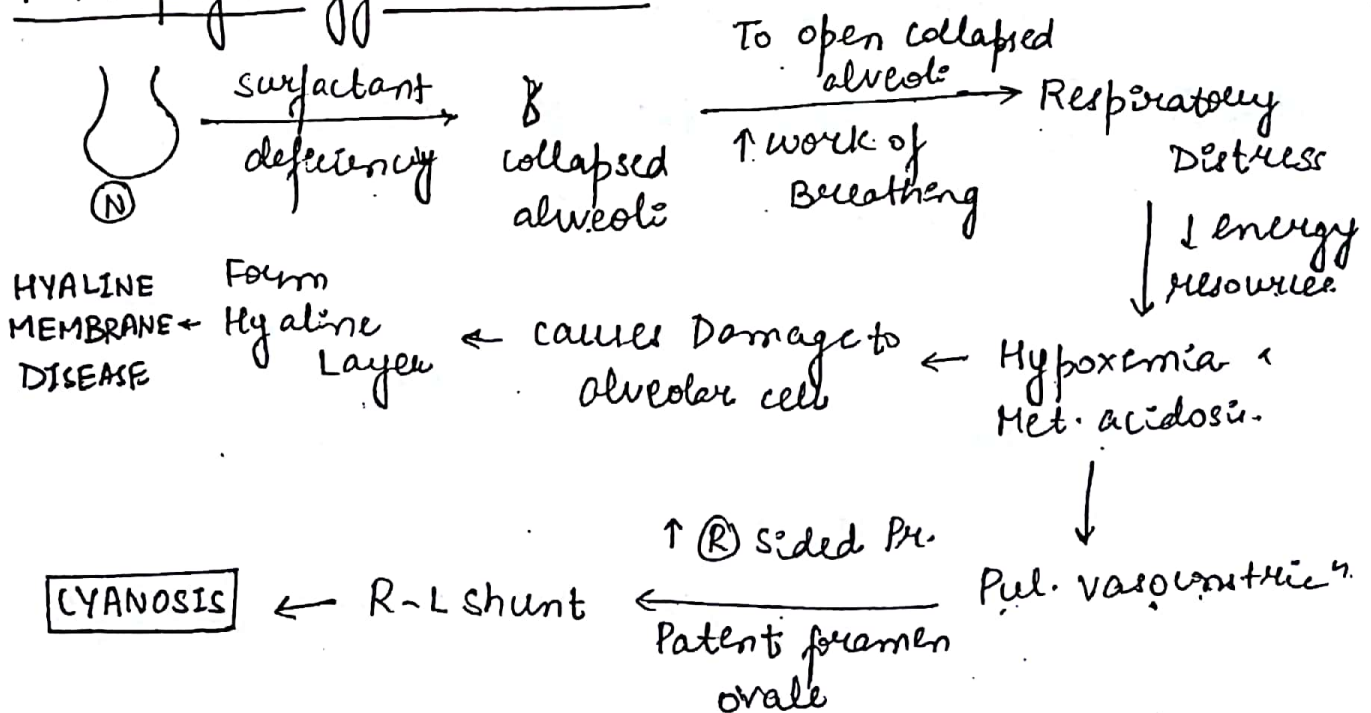
5) Functions:-

- a) surface Tension ↓
- b) maintain alveolar stability / FRC
- c) Compliance

6) Surfactant producⁿ starts at 20wk
Peak at 35wk

So, if $< 35 \text{ wk}$ \Rightarrow Respiratory distress syndrome
or
Hyaline membrane Disease.

Pathophysiology of RDS



X-Ray Findings:-

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- 1) Reticulo ~~granular~~ granular pattern
- 2) Ground glassing
- 3) white out lungs
- 4) ↓ lung volume
(↓↓ FRC)

Inv:-

Lecithin > 2 ⇒ **MATURE LUNG**
Sphingomyelin

Rx:- mild to moderate ⇒ **O₂ + CPAP**

Severe ⇒ **Invasive Mech. ventilation +
Surfactant ~~Deficien~~ Replacement**

~~Surfact~~ [Hyaline appears pink on Biopsy]

PULMONARY ALVEOLAR PROTEINOSIS

Surfactant clearance is impaired

Etiology:- **1° form** (HIC) - Auto Ab against **GM-CSF**

2° form →
✓ Acute Silicosis
✓ Haematopoietic malignancy
✓ Immunodeficiency

Silica particles are toxic to alveolar macrophage
Chr. Silicosis pt. are prone to TB.

In malignancy, macrophages are not matured enough
to carry out funcⁿ.

In immunodeficiency, macrophages ↓

Pathophysiology-

↓ Diffusion ^{for} ~~from~~ $O_2 \rightarrow$ Hypoxemia.

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Δ :-

1) Broncho ^{alveolar} ~~pulmonary~~ Lavage \rightarrow milky white

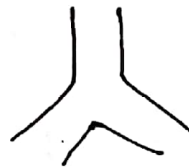
2) BAL \leftrightarrow PAS +ve

3) CT Chest \rightarrow CRAZY PAVING PATTERN

Rx - Whole Lung Lavage

WIEBELS LUNG MODEL

Trachea $\xrightarrow[Generation]{23}$ Alveoli



Functional / ventilatory unit /

Acinus = Distal to terminal Bronchiole

Radiological unit / 2° Pulmonary Lobule

= Roof of ~~ac~~ group of acinus (5-7)

↑
involved in EMPHYSEMA

Trachea



Principal Bronchus



Lobar Bronchus



Segmental Bronchus



Terminal Bronchiole



Respiratory Bronchiole



Alveolar duct & sac

upto terminal Bronchiole = Conducting Pathway

Ⓐ Main Bronchus

Aspiration is more common
this side as it is short,
stout, straight

Ⓑ Main Bronchus

Bronchiectasis more common
in Ⓑ lower part \rightarrow narrow
angulated
& drainage

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✓ (R) Lower Lobe surface
✓ seg or (R) upper

Post

Asp. Pneumonia in sitting/standing
= (R) Lower Lobe posterior Basal

Asp. Pneumonia in Bending forward
 (R) middle lobe

Bronchoscopy

HEMOPTYSIS

Lung $\left\{ \begin{array}{l} \text{High Pr. Systemic circulation} \Rightarrow \text{Bronchial artery} \\ \text{Low Pr. Pulmonary} \Rightarrow \text{Pulmonary artery} \end{array} \right.$

M/c source of hemoptysis \rightarrow Bronchial artery

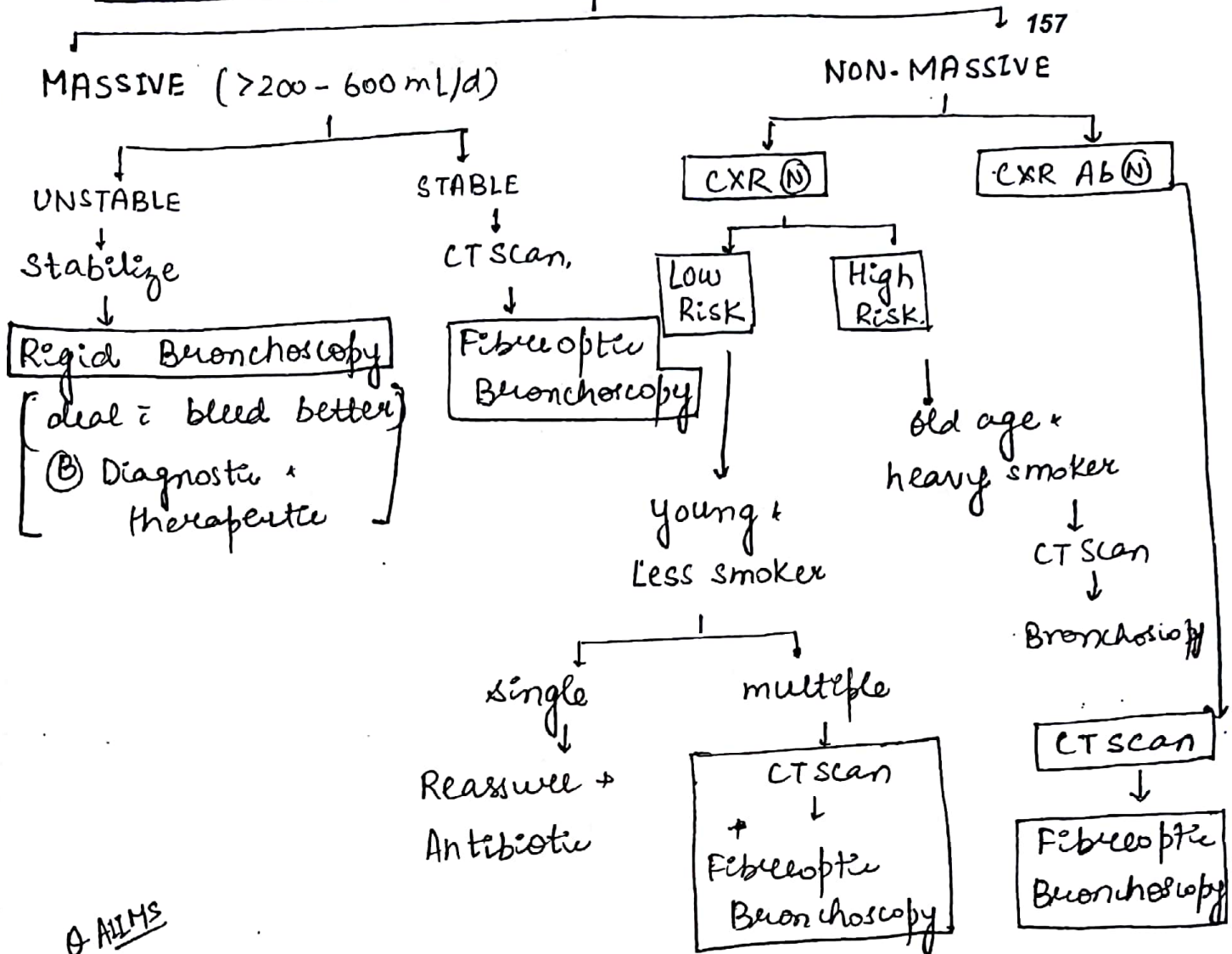
H/c source of massive hemoptysis ↑

M/c of hemoptysis in India \rightarrow TB

Muc of " worldwide \rightarrow TB

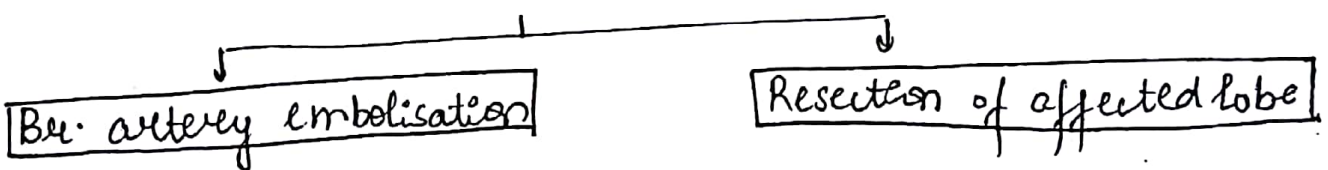
M/c of Death in massive hemoptysis \rightarrow Asphyxiation. \bar{c} Blood clot.

APPROACH TO HEMOPTYSIS



AIMS

PERSISTENT CASES-



Source of hemoptysis in Mitral Stenosis =

[Rupture of Pulmonary Bronchial
venous connecⁿ → Br. veins]

Source of hemoptysis in Pulmonary embolism → Pulmonary artery

M/c Source of hemoptysis in TB → Br. artery

Rasmussen's aneurysm → Pulmonary artery
Rasmussen's

organism that causes pseudohemoptysis

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= Serratia marcescens

INTRAPLEURAL PR.

Lung always tries to collapse to centre

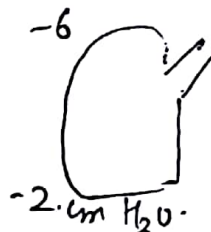
Chest wall always tries to move outward

↓
There is a Balancing Force Between the 2

⇓
-ve Intrapleural Pressure (IPP)

[usually -ve during (N) respiration
Maintains equilibrium Lung volume \Rightarrow FRC / Relaxing volume]

(N) value = -2 to -6 cm H₂O.



More -ve IPP

Deep Inspiration.

Pulley

Collapse

Fibrosis

Less -ve IPP / +ve IPP

1) Forced Expiration.

* cough, valsalva manoeuvre

2) Pushing lesions

* Tension Pneumothorax

* Manoeuvres

COMPLIANCE

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→ Stretchability of Lung.

→ Change in unit volume per unit change in pressure

$$C = \frac{\Delta V}{\Delta P}$$

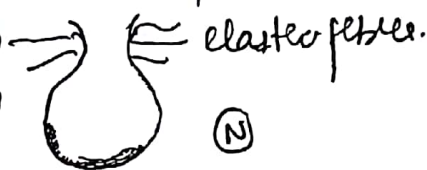
Static compliance = air flow & resistance not considered

Dynamic → air flow & resistance considered

EMPHYSEMA PATHOPHYSIOLOGY

Insp: Exp. = 2s: 3s

early closure

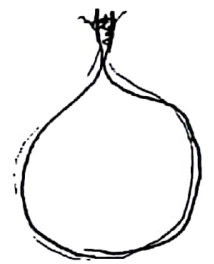


End expiration

If elastic fibres Damaged.



Air Trapping



Dynamic Hyperinflation

Emphysema at end expiration.

↓ diameter of airway

↑ Airway resistance



↓ Dynamic compliance in emphysema

Loss of elastic fibres
↓
↑ static compliance

CXR

1) B/L ~~Flt~~ Hypertranslucency

2) Flat Diaphragm

3) Tubular Heart

4) Barrel shaped chest wall

Emphysema -
RV ↑

FRC ↑

TLCT

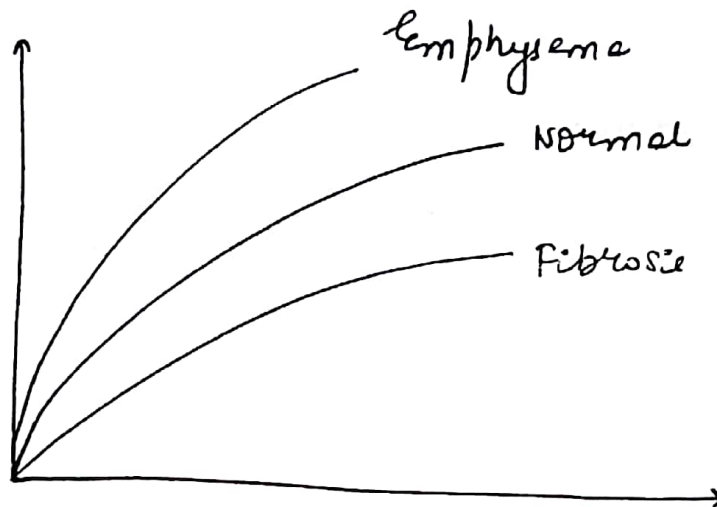
↓ compliance

↑ Compliance

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- 1) Surfactant Deficiency
- 2) ARDS
- 3) Pulmonary oedema
- 4) Fibrosis / ILD
- 5) 100% O_2 damage

- 1) old age
 - 2) emphysema
- Static comp ↑
Dynamic comp ↓ (↑ airway resistance)



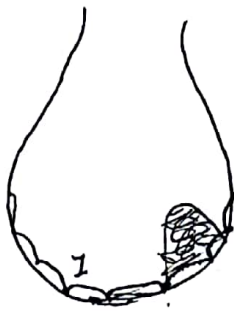
HOOVER'S SIGN → Paradoxical inward movement of lower ribcage during inspiration
severe COPD ↓
since diaphragm is not there, that's why.

HISTOLOGY OF ALVEOLI

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TYPE I

Pavement epithelium
Vulnerable to damage
More surface area



TYPE II

Secretes surfactant
Can divide & reconstitute
Type I cells
More No.

ZONES OF LUNG

Vertical regions based on hydrostatic pressure

P_A = alveolar pressure

P_a = arterial "

P_v = venous "

Zone 1 = $P_A > P_a > P_v$

2 = $P_a > P_A > P_v$

3 = $P_a > P_v > P_A$

$P_A > P_a > P_v$

$P_a > P_A > P_v$

$P_a > P_v > P_A$

(N) Lung = combination of Zone II & III.

DEAD SPACE =

Area ventilated but no sufficient gas exchange (blood flow)

Anatomical D.S.

Ext. nares upto Terminal
Bronchiole.

Measured by Fowler's method

N_2 used

Physiologic D.S.

$PDs = \text{Anat DS} + \text{Alveolar D.S.}$

In (N) Alveolar D.S. = 0

(N) P.D.S. = Anat D.S.

* Bohr's Equation

↑ Anat D.S.

- 1> Neck Extension
- 2> Bronchodilation
- 3> old age

↓ Anat D.S.

- 1> Neck Flexion
- 2> Bronchoconstriction

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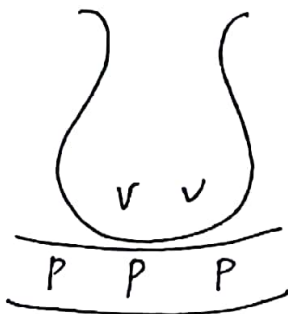
3> Endotracheal intubation /

Tracheostomy

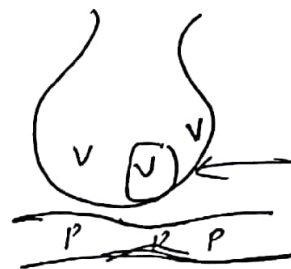
Bypass . . .
hard airway

Bypass oral,
nasal airway.

↑↑ Alv. D.S.



COPD



wasted ventilation
=

P. Embolism



In P. embolism, predominant Defect is in Perfusion

MECHANISMS OF HYPOXEMIA

① V/P mismatch (H/C)

② Shunt

③ Diffusion Defect

④ Hypoventilation

② SHUNT-

Bypass of blood w/out oxygenation.
(Diversion)

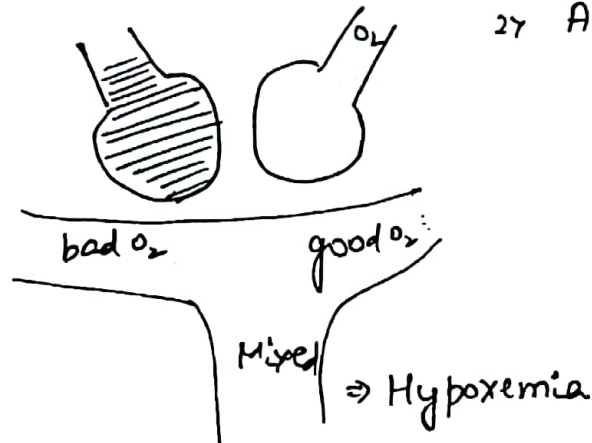
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INTRACARDIAC
② → ④ shunt

INTRAPULMONARY

1) sev. Pneumonia

2) ARDS



Less responsive to supplemental O₂.

R_x = Mechanical Ventilation.

R_x infection.

Cure pathology.

$\frac{V}{P}$ Ratio

Max. Ventilation
Max. Perfusion
Min. V/P ratio

BASE

APEX
Min. ventilation
Min. Perfusion
Max. V/P ratio

	$\frac{V}{P}$	$\frac{V}{P}$	$\frac{V}{P}$	$\frac{PAO_2}{P}$	$\frac{PA_{CO_2}}{P}$
APEX	2L	0.5L	4.	130	28
MIDZONE	4L	5L	0.8	104	35
BASE	6L	10L	0.6	92	42

1° TB \Rightarrow Mid + Lower Lobe

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2° TB \Rightarrow Apex.

\hookrightarrow active disease due to proliferation of Bacilli
Reason

\uparrow O_2 tension

\uparrow V/P Hctco.

DIFFUSION CAPACITY OF LUNG \bar{V}_{CO} (DLCO)

\downarrow DLCO

1) Fibrosis •/ILD

2) Severe emphysema

3) Pneumonia

4) ARDS

5) Sarcoidosis

6) P. Embolism

7) Anaemia

8) Pul. HTN

No blood for exchange



\uparrow DLCO

1) Polycythemia

2) Exercise (\uparrow Blood flow)

3) Alveolar H₂O

\hookrightarrow good posteur's
Wegener

4) B Acute Asthma

\uparrow eosinophil inflammation

No product

P. vasodilatation

\uparrow DLCO

New
FeNO = Test for Acute Asthma

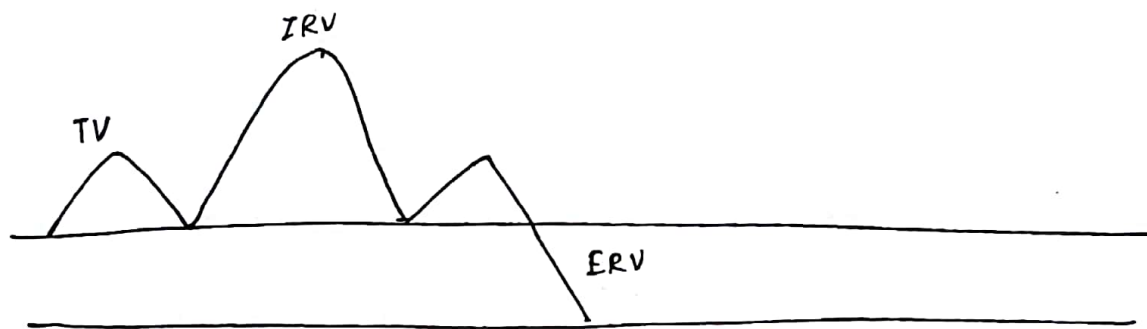
SPIROMETRY

Tidal volume = Normally in/out = 500¹⁶⁵ mL

IRV = air accommodated in effort after 1 Tidal inhalation = 3000 mL

ERV = air expelled in effort after Tidal expiration = 1100 mL

RV = Air that remains after ~~flex~~ possible expiration = 1200 mL



VC = Volume expelled forcibly after max. inhalation.

$$TV + ERV + IRV$$

$$Ic = TV + IRV$$

$$FRC = ERV + RV$$

$$TLC = \underbrace{TV + IRV}_{Ic} + \underbrace{ERV + RV}_{FRC}$$

VC

Conventional Spirometer = can't measure

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→ RV

→ FRC

→ TLC

Methods for $\left. \begin{matrix} RV \\ FRC \\ TLC \end{matrix} \right\}$

He Dilution Method

N₂ washout

Body Plethysmography. (Best)

DYNAMIC LUNG VOL

1> Forced Vital Capacity = Rapid + forcible VE

2> Timed Vital Capacity $\left\{ \begin{array}{l} \boxed{FEV_1} = FVC @ \text{end of 1st sec} = 80\% \\ \boxed{FEV_2} = FVC @ \text{end of 2nd sec} = 90\% \\ \boxed{FEV_3} = FVC @ \text{end of 3rd sec} = 98\% \end{array} \right.$

3> PEFR = Peak expiratory Flow Rate

→ Peak of FVE

→ Indicates Large airflow flow

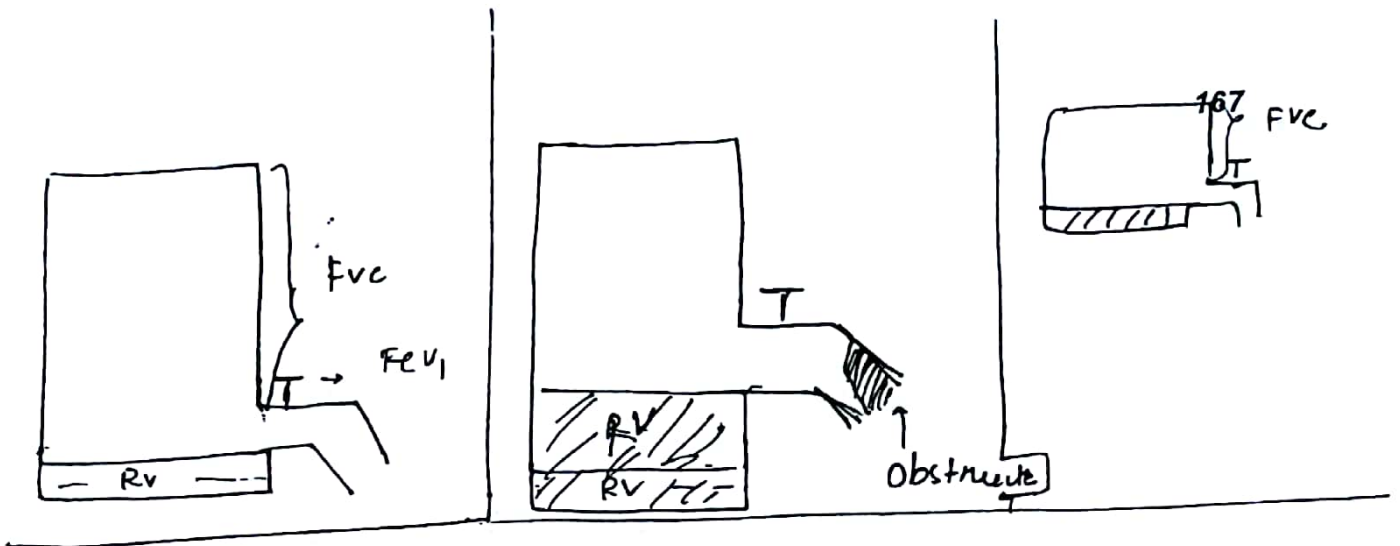
→ 400-500 mL/min

4> MEFR → Avg. velocity during mid portion of exhalation.

→ sensitive indication of small airway function

→ 300 mL/min

<u>(N)</u>	<u>OBSTRUCTIVE</u>	<u>RESTRICTIVE</u>
FVC (N)	FEV ₁ ↓↓	FEV ₁ (N) ↓
FEV ₁ (N)	FVC (N)	FVC ↓↓↓
$\frac{FEV_1}{FVC} = (N)$	$\frac{FEV_1}{FVC} = ↓↓$	$\frac{FEV_1}{FVC} = ↑/(N)$



OBSTRUCTIVE

- 1) Asthma
- 2) Bronchiectasis
- 3) COPD
 - ChC. Bronchitis
 - Emphysema

RESTRICTIVE

- Intensive RLD
 - Pul. parenchyma involved
- Extensive RLD
 - Pul. parenchyma uninvolved.

- 1) Fibrosis
- 2) Pneumonia
- 3) Sarcoidosis
- 4) Occupational lung disease

- 1) Kyphoscoliosis
- 2) Neuromuscular Disease
 - a) GBS
 - b) Polio myelitis
 - c) Myasthenia Gravis
 - d) Amy. Lat Sclerosis
- 3) Diaphragmatic Dysfunction

EMPHYSEMA

FIBROSIS/ILD

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1) Obstructive

1) Restrictive

2) $\frac{FEV_1}{FVC} \downarrow$

2) $\frac{FEV_1}{FVC} \uparrow/\text{N}$

3) $RV \uparrow, FRC \uparrow, TLC \uparrow$

3) $RV \downarrow, FRC \downarrow, TLC \downarrow$

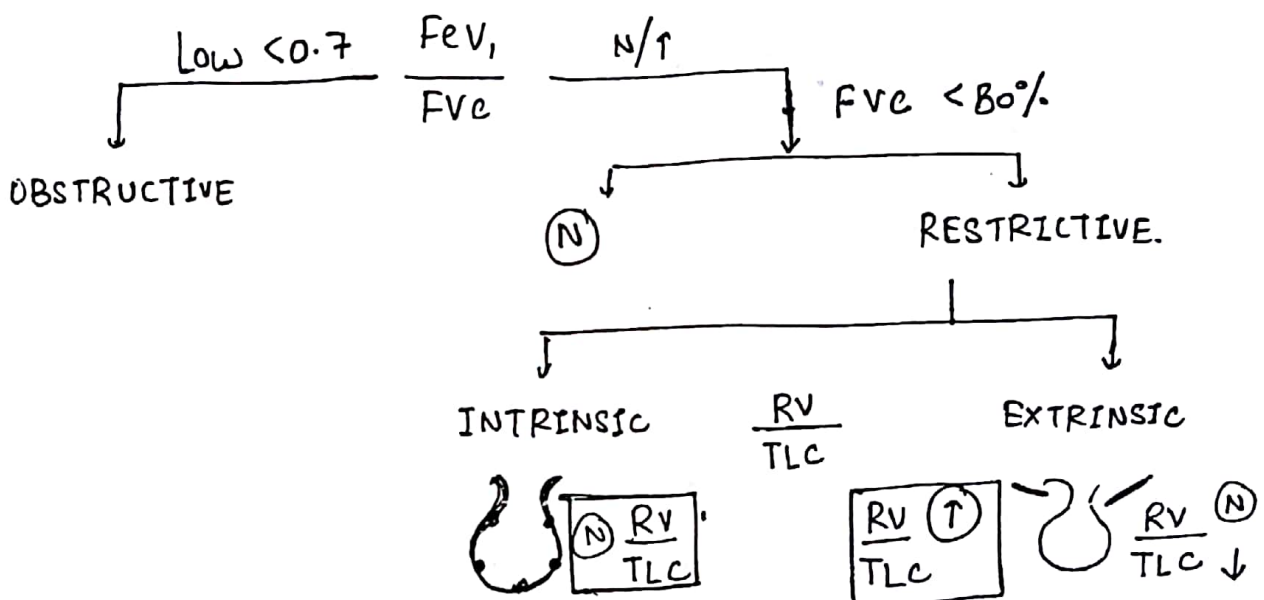
4) Compliance

4) Compliance \downarrow

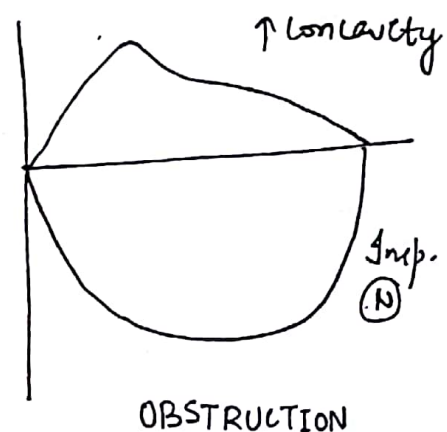
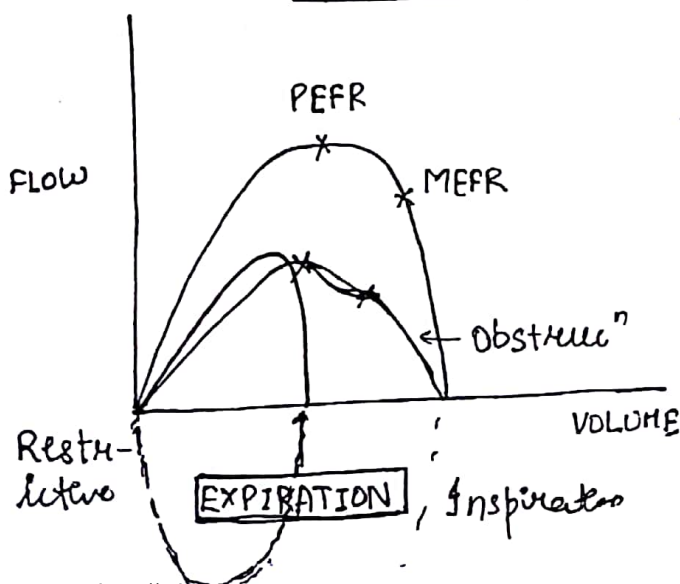
Static (↑) $DLCO \downarrow$ Dynamic (↓)

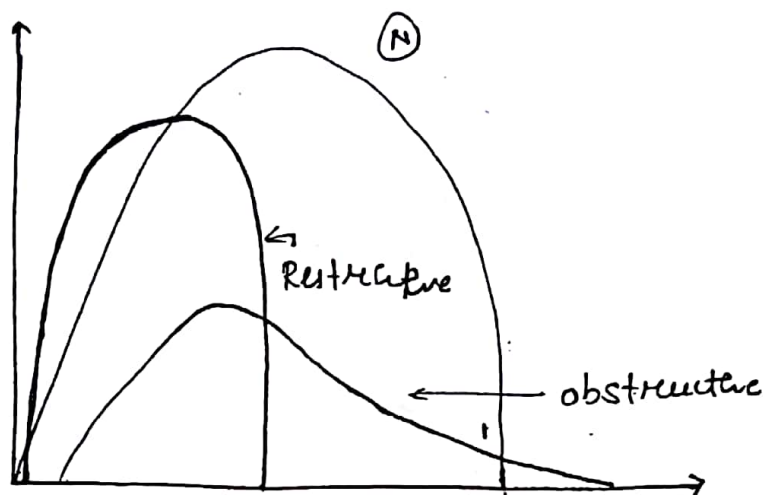
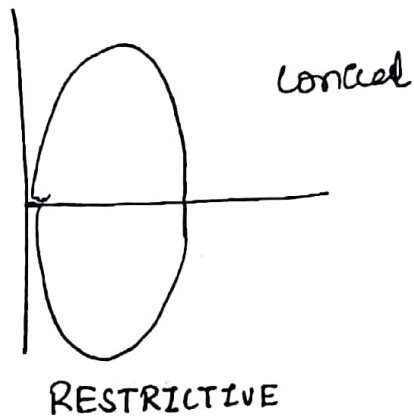
5) $DLCO \downarrow$

INTERPRETATION OF SPIROMETRY



FLOW VOLUME LOOPS



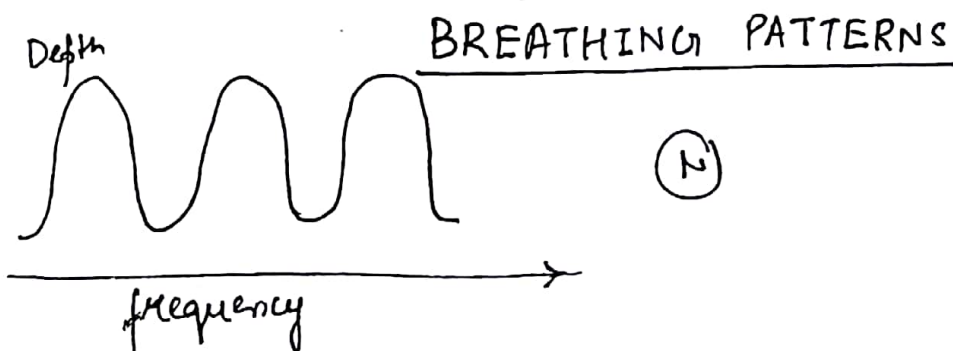


$$\text{If } FEV_1, (N), \text{ FEV } FVC (N), \frac{FEV_1}{FVC} (N) \Rightarrow \text{ (N) }$$

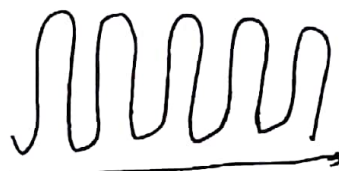
↓ SpO_2 on ~~exam~~ exertion

↓ DLCO (young ♀)

↓ Pulmonary HTN



1) KUSSMAUL'S BREATHING :-
Rapid 'Deep' Breathing

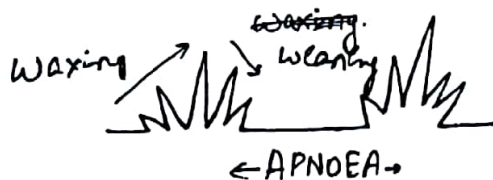


eg. sev. Metabolic acidosis \rightarrow DKA, Uraemia

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2) CHEYNE STOKES BREATHING.

\rightarrow Periodic Breathing \bar{c} cyclical Pattern.



\rightarrow altered response to CO_2 .

eg. CHF, narcotic overdose, Head injury

3) BIOTS BREATHING

\rightarrow Irregular respiration \bar{c} Apnoea

eg. Meningitis
 \uparrow ICP



4) ATAXIC BREATHING

Irregularly irregular respⁿ \bar{c} \uparrow Apnoea



eg. Brainstem injury.

BREATH SOUNDS

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(N)

- Vesicular Breathing
- Similar to sounds of rustling of leaves
- Low pitch, soft

I:E = 3:1
No pause

Ab (N)

Bronchial Breathing
Similar to tracheal sound

High pitch, Harsh

I:E = 1:1
pause

1> Tubular Breathing → Consolidation

2> Cavernous → Cavity

3> Amphoric → Metallic quality
eg. Bronchopleural fistula

ADVENTITIOUS BREATH SOUNDS :-

WHEEZE (musical)

Produced when airflow past an obstruction due to vibration of airways

Monophonic
Local involvement

eg.
Bronchial Tumour

Polyphonic
Diffuse involvement

eg.
Asthma, COPD

Rhonchi :- Low pitch wheeze

CREPTS/ CRACKLES/ RALES
Non-musical sounds

1> when air flows into secretions

⇒ Bubbling noise
cause crepts
Bronchiectasis

2> when alveoli suddenly pop open during inspiration



velcro crepts
Fine crepts

(B) Fine & Course Crepts

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- 1) P. oedema (fine & coarse)
- 2) Pneumonia
- 3) TB

STRIDOR - Loud, audible, inspiratory & expiratory wheeze
due to Laryngospasm

F.B.

Laryngeal oedema

Subglottic stenosis

~~LES~~

↓		
PULLING	NO PULL/PUSH	PUSHING LESION
Collapse Fibrosis	Consolidation	Pleural effusion Pneumothorax
<u>Percussion</u> = Dull in collapse Impaired in fibrosis	Dull note	Stony dull in P. eff. Hyper-resonant/Tympanic in pneumothorax
<u>Ascultation</u> Bs ⊖ in collapse Bs ↓ in fibrosis	Bronchial Breathing ⊕	Bs ↓ to ⊖
<u>CXR</u> collapse - Homogenous white Fibrosis - Heterogeneously white	Air Broncho gram	Pl. eff = white meniscoid fluid level. Pneumothorax = Black ⊕ compressed lung margin

PLEURAL EFFUSION

HYDROPNUMOTHORAX

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Straight line of Dullness (-)

(+)

Shifting Dullness (-)

(+)

Succession splash (-)

(+)

Sound of coin. (-)

(+)

RESPIRATORY FAILURE

Low $PO_2 < 60 \text{ mmHg}$, High $PaCO_2 > 45 \text{ mmHg}$.
(HYPOXIA) (HYPERCAPNIA)

Type I RF - Hypoxemic RF

Type II RF - Hypercapnic RF

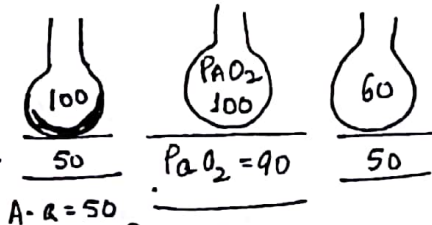
Type III RF - Perioperative RF due to lung atelectasis associated with general anaesthesia

Type IV RF - due to hypoperfusion of respiratory mls due to shock.

TYPE I

Diffusion Defect

↓ Transfer of O_2 .



$A-a = 50$

$PAO_2 = 100$
 $PaO_2 = 90$
 $PAO_2 = 60$
 $PaO_2 = 10 \text{ mmHg}$

$PAO_2 = (N)$

$PaO_2 = \downarrow$

$P(A-a)O_2 = \uparrow\uparrow$

$PaCO_2 = (N)/\downarrow$

TYPE II

Hypoventilation

↓ Resp. Effort

$PAO_2 = \downarrow$

$PaO_2 = \downarrow$

$P(A-a)O_2 = (N)$

$PaCO_2 = \uparrow$

pH $\downarrow\downarrow$ (Resp. Acidosis)

CAUSES

Pneumonia

ARDS

ILD

Pulmonary edema

P. Thromboembolism [Highest $PA-aO_2$]

Rx O_2 + Rx of underlying disease

If pt. not improving
Pneumonia

ARDS

Invasive +ve pressure
ventilation preferred

CENTRAL CAUSE

Narcotic use

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Head injury

OBSTRUCTION

F.B.

Severe COPD

PERIPHERAL

Neuromuscular Disorder

DIAPHRAGM CAUSE

Palsy

⇒ [COPD] - pneumothorax

O_2 + Rx underlying cause

If pt not improving
[COPD / NMD]

Non-invasive +ve pressure
ventilation is 1st choice

NIPPV { BiPAP (NIV commonly used)
CPAP

If no response ⇒ IPPV

C/I of non-Invasive Ventilation

- 1) Altered sensorium
- 2) ↑ chances of aspiration
- 3) Cardiac arrest
- 4) Hemodynamically unstable
- 5) Unco-operative pts.

6) Claustrophobic

7) Active GI Bleed 175

8) Recent Facial Trauma or Sx

ARDS

Defⁿ :- Acute shortness of Breath + Hypoxemia + Diffuse Pulmonary infiltrate

CAUSES:-

DIRECT

- 1) Pneumonia
- 2) Aspirationg gastric contents
- 3) Lung contusion
- 4) Near drowning
- 5) Toxin inhalation

INDIRECT

- 1) Sepsis (M/I).
- 2) Severe trauma
- 3) ~~Blood~~ multiple Blood Transfusion.
- 4) Severe Burns.
- 5) Pancreatitis

OTHER NAMES :-

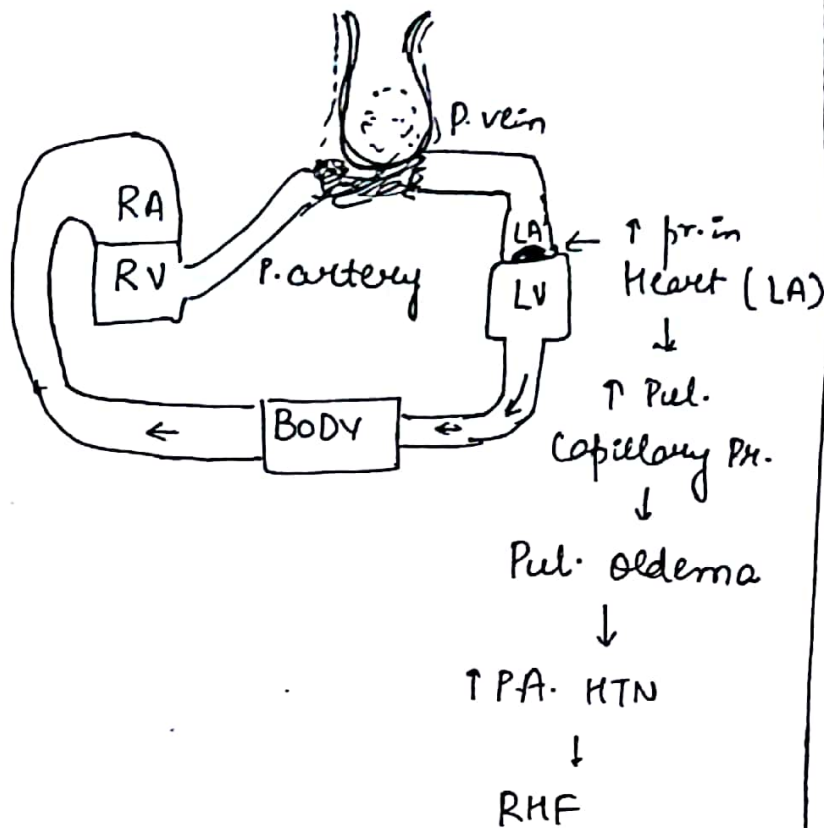
- 1> Noncardiogenic Pul. edema
- 2> ↑ permeability Pul. "
- 3> Low pressure Pul. "
- 4> Diffuse Alveolar Damage (most characteristic)
- 5> Shock Lung
- 6> Wet Lung

Pathogenesis

Cardiogenic P. edema

Non-cardiogen P. Edema

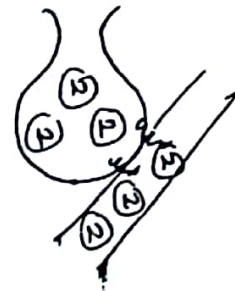
CARDIOGENIC P. Edema



PCWP = ↑ in CPE.

NON - CARDIOGENIC

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Damage to capillary endothelium & alveolar epithelium.

↑ Neutrophil entry = inflammation.

& damage = ↑ inflammatory exudate.

SHOCK LUNG.

PCWP / Pul. Arterial Occlusion Pressure

→ Swan Ganz Catheter used

→ Indirect measure of LAP

→ In CPE PCWP > 18 mmHg

In NCPE PCWP < 18 mmHg

Ass: Berlin 2012 Definition

1) Acute Onset < 7 day

2) Origin of edema → non-cardiogenic & PCWP < 18 mmHg

3) B/L diffuse infiltrate in CXR - PA

4) $\frac{P_{aO_2}}{F_{iO_2}} < \frac{60 \text{ mmHg}}{0.2} = < 300$

$\frac{PaO_2}{FiO_2}$ 200 - 300 = Mild ARDS

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$\frac{PaO_2}{FiO_2}$ 100 - 200 = Mod. ARDS

$\frac{PaO_2}{FiO_2}$ < 100 = Severe ARDS

Rx Most Recommended Strategy / Beneficial :-

1) Low Tidal Volume Mechanical Ventilation (4-6 mL/kg Body wt.)

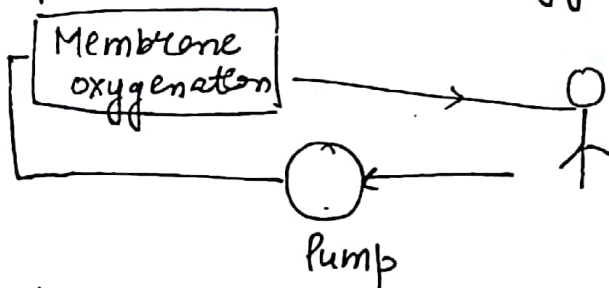
- Assist control mode to avoid ventilation associated Lung Injury

2) Adequate +ve End Expiratory Pressure

3) Glucocorticoid may be helpful.

*Newer Ventilation Modes:-

1) Extra corporeal Membrane Oxygenation.



Mech:- Blood is pumped into membrane oxygenator = oxygenates blood & sent back into body.
Beneficial in Severe ARDS.

2) Prone Ventilation.

MECH:- In prone ventilation, diaphragmatic pressure on lower alveoli $\downarrow \Rightarrow$ \uparrow sed alveoli for oxygenation ¹⁷⁸
~~at wt. of abdomen f'~~

For Benefit \Rightarrow Done for 16 consecutive hours.

- \rightarrow Helpful in improving oxygenation in pts \bar{c} severe Hypoxemia.
- \rightarrow Not helpful in pt. \bar{c} pre-existing chest wall deformity / severe fibrosis.

37 High Frequency Oscillator Ventilation

- \rightarrow Low tidal volume are given \bar{c} ~~less~~ ^{more} frequency
- \rightarrow Beneficial in few studies

TRALI

(Transfusion Related Acute Lung Injury)

- \rightarrow Occurs \bar{c} in or during 6hr of transfusion.
- \rightarrow Donor Plasma antibodies vs Recipient leukocytes
 - \rightarrow Mediator release
- \rightarrow Feature of ARDS

R_x = supportive

M/c of Transfusion related fatalities

P. THROMBOEMBOLISM (M/c of cor. Pulmonale)

Migration of thrombus from M/c source into Pulmonary artery¹⁷⁹
M/c source: Pelvic veins.

CAUSES

1°

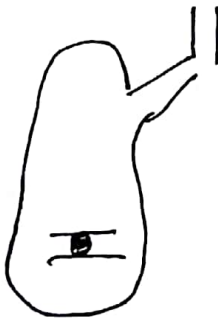
- 1) Protein C, S deficiency
- 2) Factor V Leiden mutation
- 3) Lupus anticoagulant
- 4) Antiphospholipid antibody syndrome
- 5) Hyper homocysteinuria

2°

- 1) Prolonged immobilisation
- 2) Recent Trauma. Sx
- 3) High oestrogen state
eg. ♀, estrogen containing pills
- 4) malignancy
- 5) Nephrotic syndrome

PATHOPHYSIOLOGY

LUNG



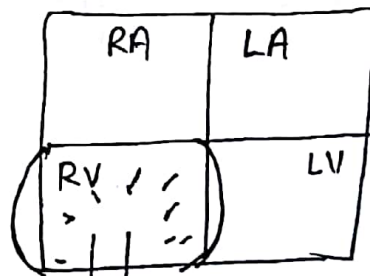
1)

↑ Pul. arterial Pressure
↳ rupture of vessel
↓
Hemoptysis

2) ↑ Alv. Dead space = Hypoxemia
↓
Shortness of Breath.

3) ↑ Serotonin by platelets
↳ Bronchoconstriction → airway ↑ Resistance

HEART



P.A.

↑ R.V. Pressure
RV Dilatation
RV Hypokinesia

Movement of septum into
LV ⇒ Ventricular

Interdependence

↓
SHOCK [COR Pulmonale]

47 Lung ischaemia \rightarrow \uparrow infl. mediators

180

5> Pleuritis \rightarrow chest pain

6> Pleural effusion \rightarrow Exudate >>
Transudate

TRIAD

- 1) ~~at~~ chest pain
- 2) SOB (H/c symptom)
- 3) Hemoptysis.

COR PULMONALE $\hat{=}$ alteration in str. & function of
② ventricle due to 1° disorder of Resp.
system including diseases of ① heart

H/c of chr. cor pulmonale \rightarrow COPD

H/c of Acute " " \rightarrow Massive PTE
 \downarrow
presents \bar{c} shock

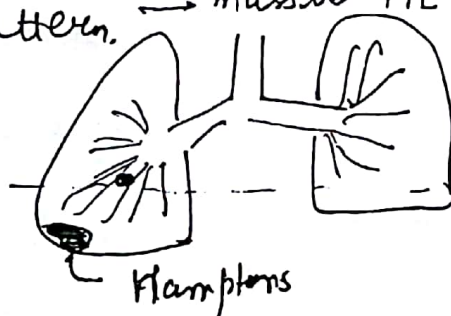
DIAGNOSIS

1> ABG \rightarrow Type I Resp. Failure

2> ECG \rightarrow H/c \rightarrow Tachycardia, T wave inversion $V_1 - V_4$

3> Most specific \rightarrow $S_1 Q_3 T_3$ pattern. \rightarrow massive PTE

4> CXR \rightarrow ② H/c
FOCAL OLIGEMIA
(Westermark sign)



2) Wedge shaped deformity above diaphragm
Hampton's hump

3) Palla's sign - Dilatation of (R) Descending Pul. artery

⇒ D-Dimer :-

Fibrin Degradation product

Elevated in PTE

Sensitive not specific

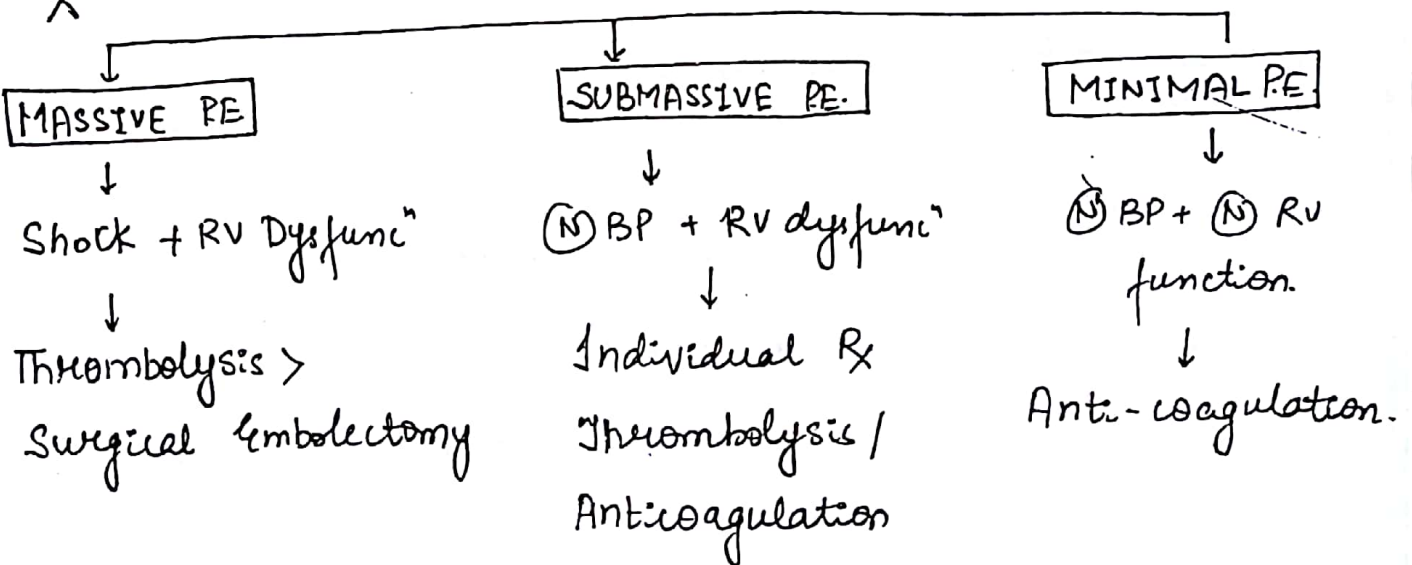
Poor predictive value but good neg. predictive value

5) Ioc ⇒ CT Pulm. Angio

6) Gold Std ⇒ Invasive Pul angiography

7) V/Q scan. - outdated ^{used in} Contrast intolerance.

Rx



PULMONARY HTN

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MPAP $> 25 \text{ mmHg}$ @ Rest

MPAP $> 30 \text{ mmHg}$ \pm exercise

MECH. WHO CLASSIFICATION

Group 1 - Direct involvement of Pul. artery

a) Heritable cause/ 1° Pul HTN - mutation in BMPR_2

↓
↑ smooth m/c proliferation

↓
young ♀.

Biopsy → Plexiform lesion.

b) Connective Tissue Disorders.

M/c cause: Scleroderma, SLE.

c) Drugs/Toxin - Fenfluramine.

Toxic Rapeseed oil

Group 2 - Due to ⊕ Heart Disease

Group 3 - Due to Resp. diseases.

COPD/ILD/Bronchiectasis/OSA

Hypoxemia → Pulm. vasoconstriction → P. HTN → Cor Pulmonale

Group 4 - Due to chronic thromboembolic events in Pulm. circulation.

Group 5 - Miscellaneous / unclear cause

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Sarcoidosis

Sickle cell Disease

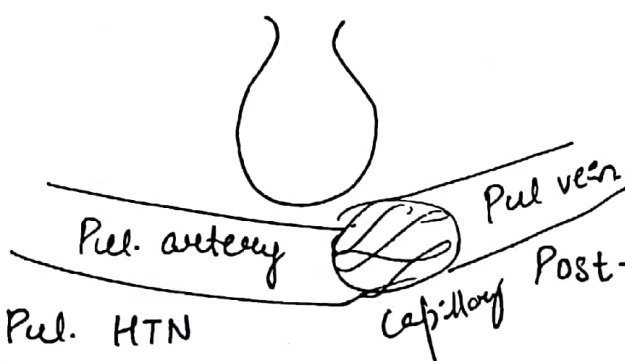
Langerhans cell histiocytosis / Eosinophilic

Lymphangiomatosis

Lymphangioleiomyomatosis

granuloma

(minkmer)



Pre-cap Pul. HTN

Group (1), (3), (4)

MPAP > 25 mmHg

PCWP < 15 mmHg

Post-capillary Pul. HTN

Group (2)

MPAP > 25 mmHg

PCWP > 15 mmHg

Rx

Group (1) & Refractory cases from other groups

Other Groups

Rx underlying disease

1) CCB - Nifedipine (now not used frequently)

2) PDE 5 Inhibitor

Sildenafil

Tadalafil

3) Endothelin Receptor Antagonist

Bosentan

Ambrisentan

4) Prostaglandin -
Epoprostenol (Iv)
Flaprost (Inhaled)

5) Guanylate cyclase activator
Receptor

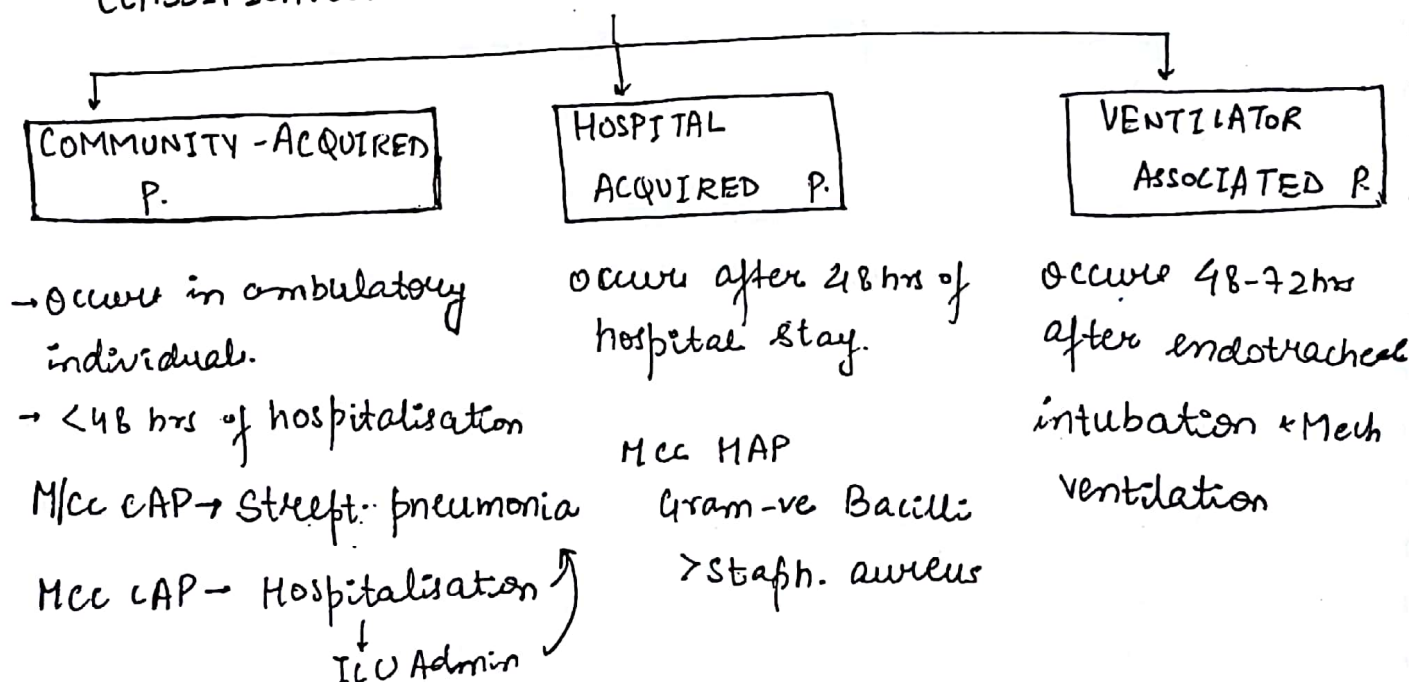
DOC for Low Risk Cases :- Initial monotherapy of
either PD5 Inhibitor
or ETRA
↓
followed by combination Rx.

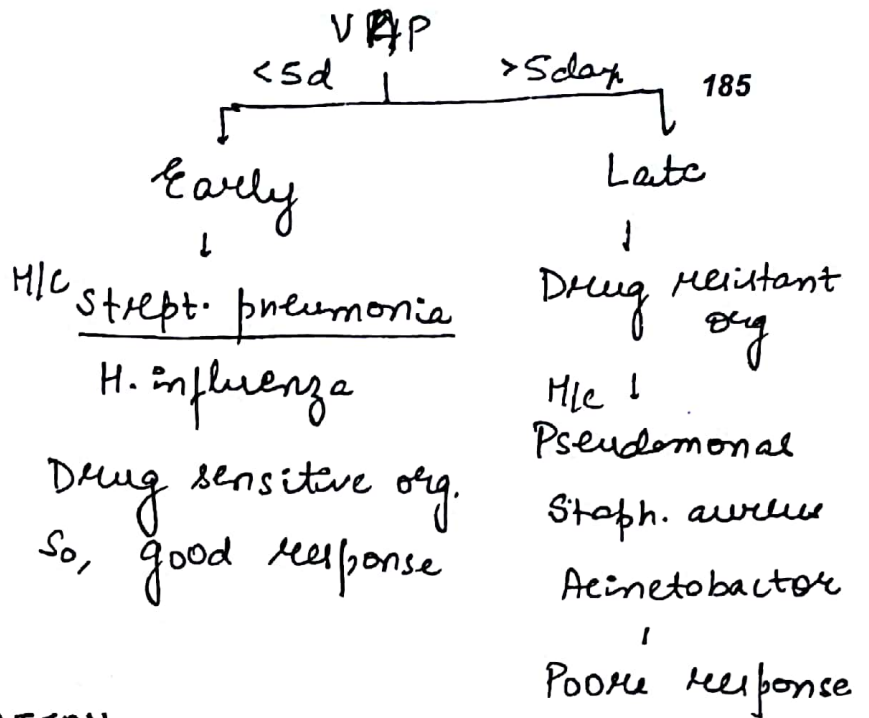
Doc for High Risk / Emergency & Prostacyclins
(Symptoms at Rest)

PNEUMONIA

Acute resp illness characterised by Radiological Pulmonary shadowing.

CLASSIFICATION-





CLINICAL CLASSIFICATION

TYPICAL



- Fever + Productive cough
- Predominant neutrophilic leucytosis
- Gram staining → Reveal organisms
- CXR → Alveolar exudates
- M/C - Strept. Pneumoniae
- Staph. aureus
- Klebsella
- Pseudomonas

ATYPICAL



- Interstitial Inflammation
- Fever + cough → scanty sputum
- Mild Leucocytes
- Gram staining → no organism
- CXR - NO alveolar oxidation
- Interstitial pattern
- M/C - Mycoplasma
- Legionella
- Coxiella
- Chlamydia
- Viral Pneumonia

TYPICAL PNEUMONIA


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(I) STREPT

Risk Factors } M/c {
Smokers
alcoholics
DM

c/f Red Rusty Sputum

CXR

 Localised involvement of lobe/segment

M/c pattern in CAP

Rx - β lactams

(II) STAPH

IV drug users pneumonia

Fatal pneumonia post viral illness

mucopurulent sputum

CXR



Bronchopneumonia

B/L - patchy involvement

M/c pattern in nosocomial Pneumonia

Pneumatocele + cavity + Lung abscess. may be seen

Rx MRSA = Vancomycin

VRSA = Linezolid

(III) KLEIBSELLA

Alcoholics

DM

malnourished

Red currant Jelly sputum

CXR



Bulging fissure sign

- cavities

- Dense consolidation

- Lower lobe involvement

seen if hematogenous spread

Rx -

Bleactam +

Aminoglycoside

(IV) PSEUDOMONAS

→ Frequently occurs as VAP

→ occurs as Recurrent pneumonia in
 ↑ Structural Lung disease
 → cystic fibrosis
 ↓ Bronchiectasis

→ Fever, mucopurulent secretion, Leucocytosis.

- B/L infiltration of CXR

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Rx - Two Antipseudomonal ABs of 2 different classes.

Antipseudomonal ABs ~~AB~~ β lactam + FQ (or) Aminoglycoside

ATYPICAL PNEUMONIA

MYCOPLASMA / walking P.

M/c atypical pneumonia

Eaton agent pneumonia

Man \rightarrow Man transmission.

Extrapulmonary features

1) CNS - GBS

peripheral neuropathy

2) Ear - Bullous myringitis

3) Blood - \uparrow cold agglutinins
Haemolytic anaemia

4) CVS - Myocarditis
Pericarditis

5) SKIN - Erythema Nodosum
No cell walls (+)

Rx - Macrolide / FQ / Tetracycline

LEGIONELLA

M/c mode of Transmission -

microaspiration \rightarrow aerosolization

Spreads through contaminated water

Limited man to man transmission

Special Features:-

1) Associated GI features: diarrhoea

2) " CNS features:-

confusion, headache,
high grade fever

3) Altered LFTs

4) $3-Na^+ < 130$ meq

Gram staining \rightarrow no organism

Poor response to β lactams

Old age, Immunocompromised
occurs in 10 days discharge
from hospital

Rx - FQs / Macrolide / Tetracycline

Resp FQs - Levo / Moxi

PNEUMOCYSTIS PNEUMONIA (PCP)

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M/c opportunistic infection in HIV = TB

M/c pneumonia in HIV = TB

M/cc pleural effusion in HIV = TB

M/cc fungal pneumonia in HIV = PCP

R/F:-

- 1) $CD4 < 200 / \mu L$ in HIV
- 2) Long Term Immunosuppressive Rx
- 3) Organ Transplant
- 4) 1° Immunocompromised

C/F:-

Subacute onset

Fever

Shortness of Breath

Hypoxemia

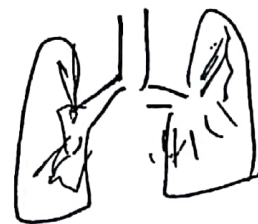
CXR:-

Perihilar infiltrates

Diffuse interstitial infiltrate

In flw - pneumatocele

Complicate a Pneumothorax



Δ :- visualize the cyst

- Wright - Giemsa
- Gomori - methamine stain.

Broncho-alveolar lavage (Best sample)

Rx = COTRIMOXAZOLE (septran)

- If sulpha allergy → 1) Clindamycin + Primaquine
2) Trimethoprim + Dapsone
3) Pentamidine
4) Atovaquone

DOC for Prophylaxis → COTRIMOXAZOLE

↓
DOC for NOCARDIOSIS.

VIRAL PNEUMONIA

BIRD FLU (H_5N_1)

- Avian Influenza
- Less M → M transmission
- Epidemic not pandemic

DOC - oseltamivir

SWINE FLU (H_1N_1)

- ↑↑ M → M transmission
- Epidemic + Pandemic

DOC - oseltamivir

75mg BD for 5 days
(neuraminidase Inhibitor)

DOC prophylaxis - oseltamivir

75mg OD for 10 days

other drugs - Zanamivir
Peramivir

ASSESSMENT of SEVERITY

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Confusion

Urea $> 7 \text{ mmol/L}$ or $> 20 \text{ mg}$

RR $> 30/\text{min}$

B - SBP $< 90 \text{ mmHg}$ DBP $< 60 \text{ mmHg}$

65 Age age > 65

0-1 \Rightarrow Home Rx + antibiotic

2 \Rightarrow Hospitalisation + Rx

3-5 \Rightarrow Consider as severe pneumonia, may require ICU admission.

EMPIRICAL REGIMEN FOR HOSPITALISED Pt OF PNEUMONIA

\Rightarrow TYPICAL + ATYPICAL
 β lactam + Macrolide

LUNG ABSCESS

191

1° Abs. form

M/c type

Due to aspiration

M/c organism - oral anaerobes



Rx - IV. clindamycin.

2° form

Occurs due to pre-existing disease process in lung

Bronchial obstruction

Immuno deficiency

Staph, Klebsiella

Rx - Broad spectrum
ABs

Strategies to Prevent VAP :-

- 1> Elevation of Head of Bed. 30°-45°
- 2> Oral Decontamination τ Chlorhexidine
- 3> Sedation vacation (\downarrow sedation)
- 4> Assessment of readiness to extubate daily
- 5> Use of NIV wherever feasible

X Frequent change of Tubes

ORAL ANAEROBES-

- Peptostreptococci
- Fusobacterium
- Bacteroides

PLEURAL

EFFUSION

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TRANSUDATE (M/c)

LIGHT'S CRITERIA

EXUDATE

$\frac{\text{Ple. fluid. Protein}}{\text{S. protein}} < 0.5$

$\frac{\text{Pl. fluid LDH}}{\text{S. LDH}} < 0.6$

$> 0.5, 0.6$

Cytology = ? malignant cells

cell count

Gram staining ? infection

TB marker = ADA,

Interferon γ

cause-

1> CHF (M/c overall)

2> Hepatic Hydrothorax

3> Nephrotic Sx

Special Features

1> Low glucose ple. fluid ($< 60 \text{ mg/\%}$)

a) Empyema

b) Malignancy

c) RA

d) TB (Rare)

2> High Amylase

a) Pancreatitis

b) oesophageal rupture

c) malignancy

3> High Lipid Ple. eff / white coloured

Chylothorax

Accumulation of

Pl. TGA $> 110 \text{ mg/\%}$ Chyle due to disruption of thoracic duct

M/c - Surgical Trauma
Malignancy

Pseudochylothorax

Accumulation of cholesterol crystals in long standing eff.

TB, RA, ch. empyema
myxoedema
cholesterol $> 200 \text{ mg/\%}$

* Parapneumonic Eff

M/c of exudative pleural eff

Eff associated with
Pneumonia
Bronchiectasis
Lung abscess

Milky white BAL
193
Alveolar Proteinosis

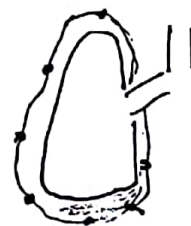
Indications of ICD insertion in parapneumonic eff :-

- 1> Pus in pleural cavity
- 2> pH < 7.2 (pleural fluid)
- 3> Ple f. glucose < 60mg%
- 4> Loculated pleural effusion
- 5> Gram staining reveals organisms

TB Effusion

- M/c exudative effusion in India

- Occurs due to hypersensitivity response to TB Bacilli in Pleural Tissue



- Exudative — Lymphocyte predominant

ADA > 40 IU

IFN γ > 140 pg/ml

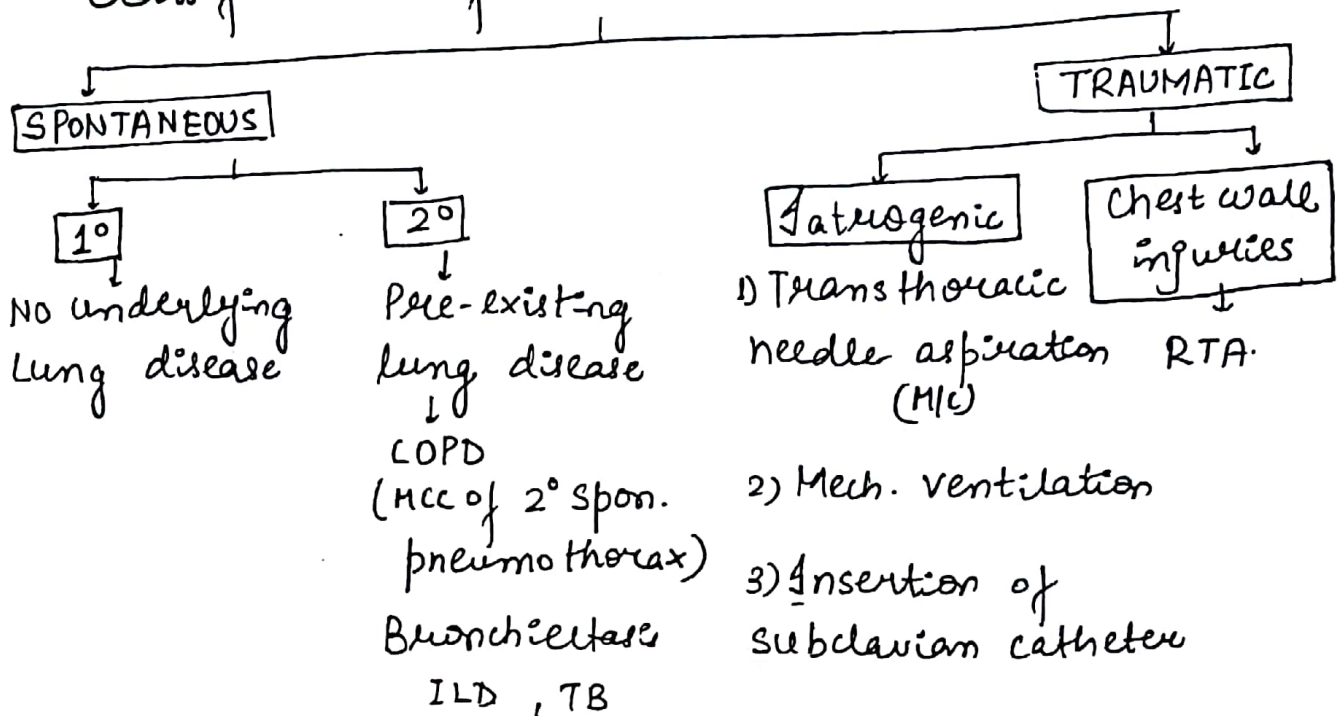
↓ mesothelial cells

- Pleural Fluid for AFB only positive in 20-30% cases.

Gold Std -

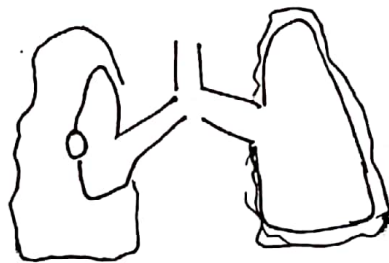
Thoracoscopic pleural Biopsy + Culture for M.tb.

Classification of Pneumothorax :-



TENSION PNEUMOTHORAX

- 1) Large air leak
- 2) Air leak serves as Ball valve (or) one way valve mechanism



- 3) ↑↑ Positive intrapleural Pressure
- 4) Compressing adj lung + mediastinal vessels

↓ VR

↓ Shock (medical emergency)

- 5) Rx - Next step / Best steps - Insertion of wide bore needle @ 2nd I.C.S. anteriorly mid clavicular line on affected side followed by ICD insertion.

High Inspiratory Pressure alarm on ventilator¹⁹⁵ can suggest ~~Press~~ Tension Pneumothorax.

Pneumo Mediastinum

Air in mediastinum

C/F - Shortness of Breath
Chest pain

HAMMAN'S Crunch → Crunching sound synchronous
to heart Beat

CXR - Continuous Diaphragm Sign.
Subcutaneous Emphysema

ASTHMA

Characterised By recurrent symptoms due to
variable & reversible bronchoconstriction caused due to
airway hyper-responsiveness to variety of stimuli

COPD - characterised by persistent symptoms & airflow
limitation due to airway & alveolar abn^o
caused by significant exposure to noxious stimuli.

ASTHMA

Allergen related
Reversible airflow limitation
Early presentation
Relief w/ Bronchodilators

COPD

Smoking related
Persistent airflow limitation
Delayed presentation
only partial response

TYPES PATHOGENESIS

EXTRINSIC / ATOPIC / ALLERGIC

Allergen related

S. IgE ↑

Skin test +ve for allergen

Mild form

Young onset

H/c allergen world

↳ HOUSE DUST MITE / Dermatophagoides

Pollen → cause Thunderstorm
Asthma

Δ:-

1) SPIROMETRY

obstructive

Broncho dilator Reversibility = \uparrow FEV₁ > 12% (or) 200cc
after SABA.

FEV₁ 65% $\xrightarrow[15\text{min}]{\text{SABA}}$ FEV₁ 80%

2) PEFR Variability

>20% diurnal variation.

3) METH. CHOLINE challenge Test / Broncho provocation Testing

fall in FEV₁ > 20% after meth. choline.

for airway hyper-responsiveness

4) FeNO > 50 PPb ≈ eosinophilic inflammation.

INTRINSIC / ~~NONALLERGIC~~ ^{196,}

NONATOPIC / IDIOSYNCRATIC

Viral infection ⇒ Trigger

S. IgE (N)

Skin test -ve for

Severe forms

Late onset

ACUTE SEVERE ASTHMA

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ClF-

1) Pt. speaks in words

2) Can't lie down

3) RR > 30/min

4) HR > 120/min

5) Bil wheeze

6) Accessory muscle use

7) Pulsus Paradoxus. → [Rapid change in intrapleural pr.]
causes this.

Functional Parameters :-

1) PEF < 50% predictive value.

2) SpO₂ < 90%

3) PaO₂ < 60 mmHg

→ Type I Resp. Failure

But Type 2 RF can occur in severe cases
↳ due to fatigue of resp. muscles.

* Life Threatening Asthma :-

1) Patient - altered sensation

2) Silent chest

3) ↓ Respiratory effort

4) PaO₂ < 60 mmHg

5) PaCO₂ ↑↑

Rx - 1) O₂ +

2) SABA + (Salbutamol) + Inhaled corticosteroid

• SAMA (Ipratropium)

2) I.V. Steroid

↳ ↓ Inflammation
↳ ↑ sensitivity of β₂ Receptor to broncho dilator

3> Theophylline now not used routinely

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4> In few cases IV MgSO₄ given

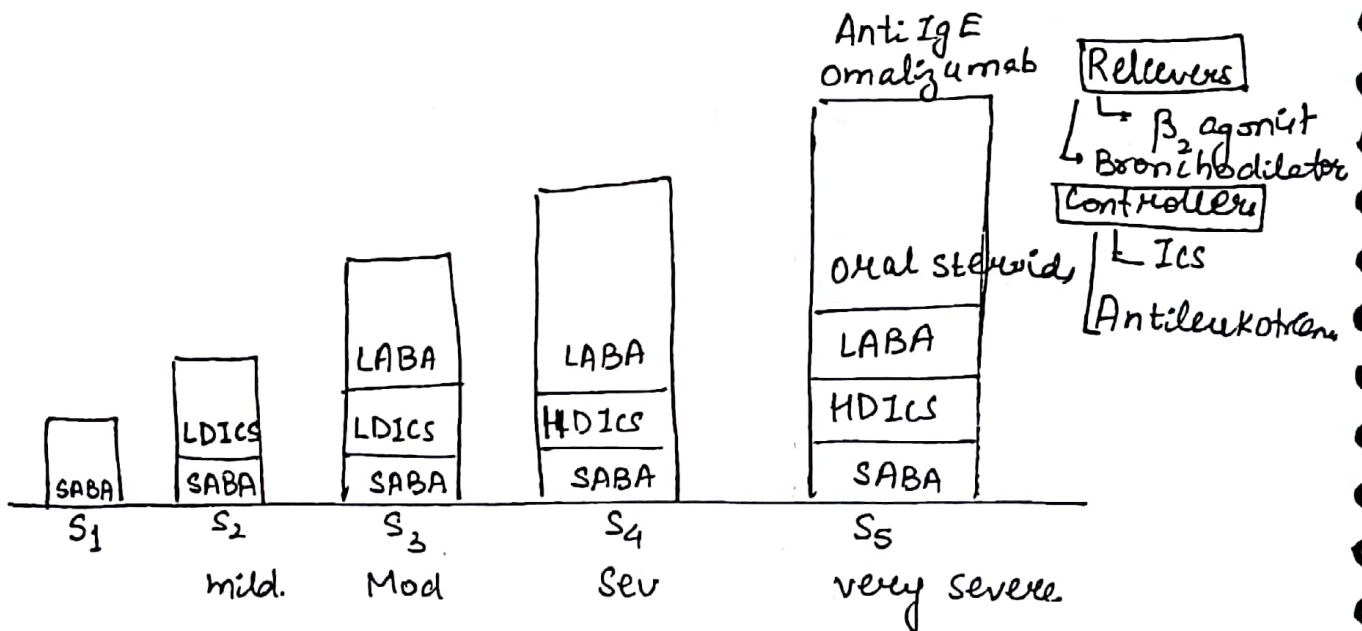
5> In deteriorating / life threatening case \Rightarrow Invasive
Mech. ventilation.

High inspiratory flow \leftarrow \rightarrow \uparrow Expiration Time
I:E = 1:3 or 1:7.

Step Wise Therapy & Classification

	Intermittent	Mild	Mod	Sev
Day Time Sx	< 2/week	> 2/week	daily	through-out day
Night time awakening	< 2/month	> 2/month	> 2/week	daily

Day Time Sx < 2/week | > 2/week | daily | through-out day
Night time awakening < 2/month | > 2/month | > 2/week | daily



LDICS \rightarrow low dose ICS.

HDICS \rightarrow High dose ICS.

Most imp. in asthma management is pt. ~~self~~ education
& active self Mx. 199

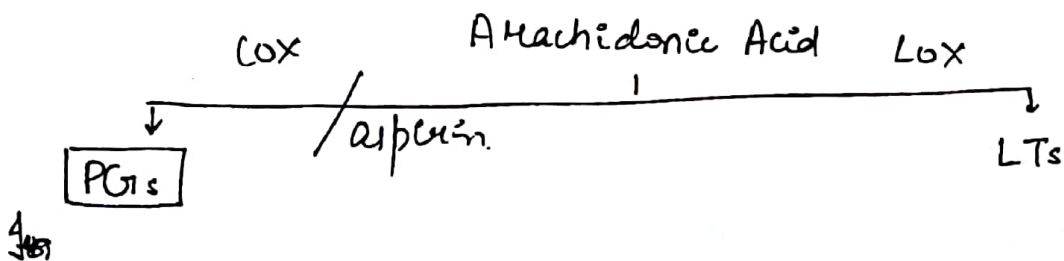
EXERCISE INDUCED ASTHMA

In susceptible individuals, exercise can induce asthma
more frequent during cold & dry climate > hot humid
condition.

Doc for short term prophylaxis = SABA > Anti-leukotrienes/
Mast cell stabilizer.

Doc for Long term prophylaxis & overall control of disease } corticosteroids

ASPIRIN INDUCED ASTHMA



Samter's TRIAD-

Nasal polyposis + Aspirin sensitivity + Asthma

In susceptible individuals, aspirin blocks COX pathway
& shifts balance towards Lox pathway \Rightarrow \uparrow LTs

\Downarrow
Bronchospasm

Rx = ICS + Aspirin BABA + Anti-leukotrienes +
Aspirin desensitization.

BRITTLE ASTHMA

Unstable Disease $\hat{=}$ **frequent exacerbations**

(N)

Lung function

Type 1 Brittle
Persistent fluctuation
in lung functions



Difficult to Rx asthma
* Oral corticosteroids
+ continuous infusion =
 β_2 agonist

Type 2 Brittle
Near normal lung
function \rightarrow Rapid
fall + death.



Localized anaphylaxis
↓
Laryngospasm

Doc :- Subcutaneous
epinephrine +
Adrenaline

CORTICOSTEROID RESISTANT ASTHMA

Poor response to Rx after 2 weeks of oral corticosteroids (40mg/day) Rx

steroid sparing drugs can be used.

Anti IgE = Omalizumab

Anti IL5 = Mepolizumab

COPD

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(CHR. BRONCHITIS:-

Cough & sputum for >3 months in 2 consecutive years

EMPHYSEMA:-

Destroy distal to terminal bronchiole.

R/F:-

- | | |
|-----------------------------------|---|
| 1) Smoking | → young age
→ Less smoking H/o
→ Family H/o - Chx. 14, AR.
→ B/L Lower predominant
→ Bronchiectasis
→ Unexplained Liver Disease. |
| 2) α_1 AT Deficiency | |
| 3) Indoor & outdoor pollution. | |
| 4) Gold exposure coal. | |
- 2)

TYPES OF EMPHYSEMA

CENTRIACINAR

occurrence Smokers
M/c overall
upper lobes

Pathology



RB involved
alveolar duct +
Sac spared

PANACINAR

α_1 AT Def.
More severe in
LL



Resp. Bronchiole +
Alv. Duct + Sac
involved

DISTAL ACINAR

Adjacent to fissure
foci.
upper $\frac{2}{3}$ rd of Lung



Resp. Bronchiole spared
Alv. duct + Sac
involved

Δ:- 17 SPIROMETRY

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$$\frac{FEV_1}{FVC} < 0.7 \approx \text{Obstructive}$$

No significant Bronchodilator reversibility

GOLD Staging (Global Initiative for obstructive Lung Disease)

I Mild	$FEV_1 / FVC < 0.7$	$FEV_1 \geq 80\%$	Pred. FEV_1
II Mod.	" " "	$FEV_1 50-79\%$	" "
III Severe	" " "	$FEV_1 30-49\%$	" "
IV very severe	" " "	$FEV_1 < 30\%$	pred. value

Prognosis Index

BMI

Obstruction (FEV_1)

Dyspnoea (MRC scale)

Exercise Capacity \Rightarrow Distance covered in 6 minute walk test

Low score \Rightarrow Good Prog.

High score \Rightarrow Poor Prog, \uparrow mortality

CHARACTER	BLUE BLOATER	PINK PUFFERS
PATHOLOGY	Ch4. Bronchitis.	Emphysema.
SYMPTOM	Cough \pm expectoration	Shortness of Breath
APPEARANCE + POSTURE	obese + comfortable at rest	lean + tachypnoea at rest
Breath sounds	Rhonchi - Noisy	Less noisy
CXR	\uparrow Interstitial Marking	Hyperinflated Lung
PFT	obstructive	obstructive

Rx:-

203

1> Smoking cessation. → most imp. intervention.

2> BRONCHODILATORS

A> LABA

B) LAMA

Ultra LABA → O.D. Dose

✓ Indacaterol

✓ Vilanterol

✓ Olodaterol

Tiotropium

Umeclidinium

Glycopyrronium.

3> STEROID :-

a) Inhaled

↓ freq. of exacerbation

b) Systemic

During exacerbation.

4> SELECTIVE PDE₄ INHIBITOR:-

Roflumilast

5> ANTIBIOTICS:-

During exacerbation (H. influenza)

6) MUCOLYTICS-

N Acetyl cysteine

7) If Hypoxemia → Long Term O₂ therapy (15 hours a day)
low flow O₂

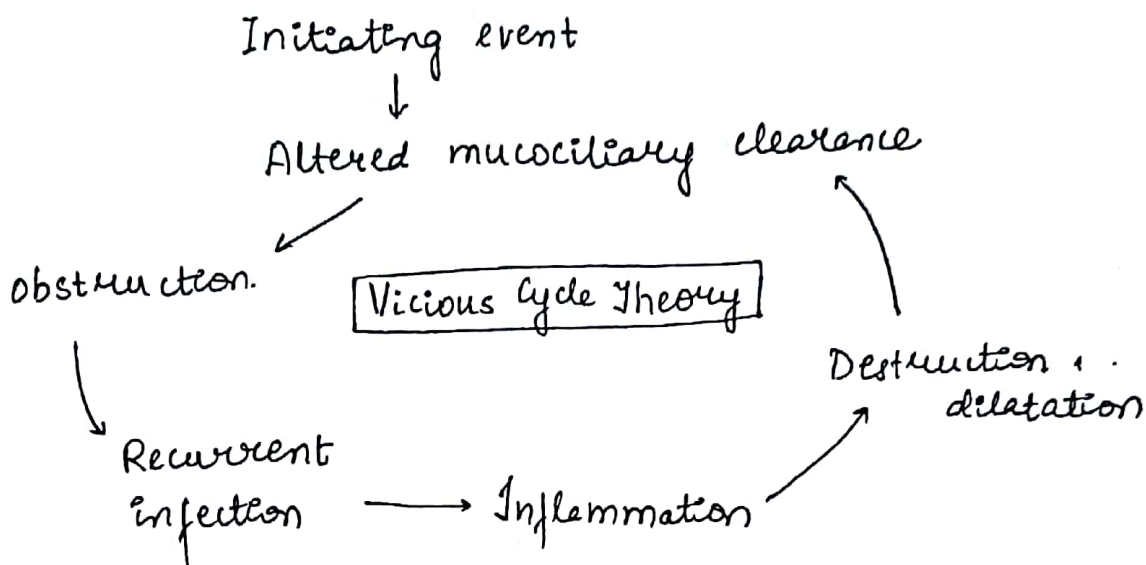
8) Lung Volume Reduction Surgery

a> LUNG TRANSPLANTATION (M/c Indication for lung transplantation is COPD)

10> During exacerbation, 1st choice - non-invasive ventilation.
> Invasive "

BRONCHIECTASIS

Ab (N) Permanent Dilatation of bronchi due to ²⁰⁴ loss of muscle & elastic tissue.



CF:-

copious sputum
coarse crepts

ETIOLOGY & MECH:-

I) BRONCHIAL OBSTRUCTION

a) **Intramural**



Tumours - Carcinoid
Sq. cell carcinoma
Small cell carcinoma

b) **Extrinsic Compression.**

Enlarged TB hilar LN can compress (R) middle lobe.
Bronchus → (R) middle lobe
collapse & bronchiectasis
↓
BROOK'S SYNDROME.

II> BRONCHIAL INJURY

A) Infection

TB, adenovirus

B) Altered Immune ²⁰⁵ Response

→ Connective Tissue Disorder

→ Allergic Bronchopulmonary Aspergillosis (ABPA)

III> TRACTION BRONCHIECTASIS in ILDs

IV> GENETIC CAUSES

A) 1° ciliary dyskinesia

B) Cystic fibrosis

C) Cartilage Defect

William Campbell's

Mounier Kuhn Syndrome

D) Yellow Nail Syndrome

Long. Lymphoedema + Yellow nail + Pleural Effusion
+ Broncheectasis

CYSTIC FIBROSIS

Inheritance - AR

Chromosome 7q

Gene - CFTR

Channel - Cl^-

Mutations - Class I - VI

M/c class II, $\Delta F508$

"Thick secretions"

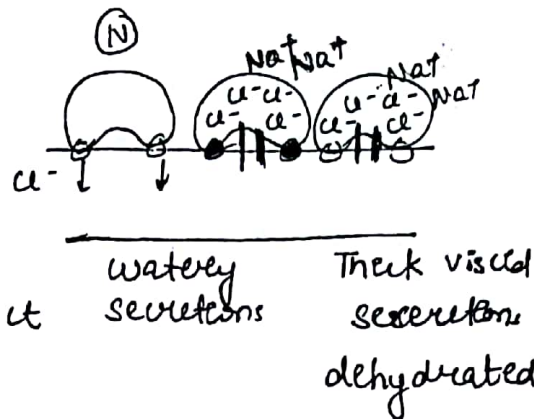
I

II

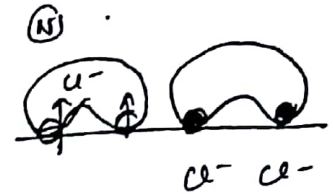
Resp. Tract

GIIT

Reproductive Tract



Sweat Gland



ENac → responsible for 'pathophysiologic process'

SCREENING Test
↑ Sweat $Cl^- > 60 \text{ mEq}$

Other Inv:-

- 1> DNA analysis for mutations
- 2> ↑ Nasal Pot^+ Difference
- 3> CFTR Gene Sequencing:- Gold Std.

SYSTEMIC MANIFESTATIONS:-

1> Respiratory Tract-

URT

Recurrent infections
Sinusitis

LRT

Recurrent pneumonia
(H/c pseudomonas), staph
Bronchiectasis, Lung abscess
Empyema, P. Thrombosis,
Resp. failure, Hypoxemia,
P. HTN, Cor Pulmonale

2) GIIT

neonate Meconium ileus.

Liver → Biliary Cirrhosis,

GB - Gall stone

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Pancreas

- Endocrine insufficiency - early manifestations
- DM, → occurs later.

3) Reproductive Tract -



In utero occlusion of vas Deferens
by thick secretions → AZOOSPERMIA.
infertile



Thick cervical secretions

Rx

17 CFTR Modulators:-

Ivacaftor - G551D mutation class III

Lumacaftor + Ivacaftor - third in class II

TYPES OF BRONCHIECTASIS -

(N)



M/C - Cylindrical



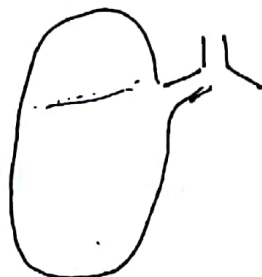
varicose



saculare

SITES of B'XIS -

→ Upper Lobe



1) Cystic fibrosis

2) TB

3) Post radiation B'XIS

2) Lower Lobe



- 1) Interstitial Lung Disease
- 2) Chx. recurrent aspiration
- 3) Immunodeficiency state

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3) Middle Lobe - non-tubercular mycobacterium.



Mycobacterium avium complex (MAC)

Rx of B'XIS-

1) Airway clearance.

Mucolytics

Chest Physiotherapy.

2) Antibiotics

During exacerbation

Prophylaxis

Long term

Azithromycin

(6 months)

Inhaled

Tobramycin

(1 month on-off)

3) Bronchodilators - ICS beneficial in some

4) If Hypoxemia \Rightarrow O_2 .

5) Localised Disease \rightarrow Sx

6) Diffused " \rightarrow Lung Transplantation.

High flow O_2 not recommended. Y?

1) Abolition of Hypoxemic resp. drive

2) High O_2 given can ~~ext~~ cause release of CO_2 from RBC

↳ HALDANE
EFFECT.

IOc :- HRET Chest

EOSINOPHILIC LUNG DISEASES

[Peripheral eosinophilia + Lung infiltrates]

CLASSIFICATION

Unknown cause

1) Acute eosinophilic pneumonia

2) Chronic " "

3) Hypereosinophilic Syndrome

4) Churg Strauss Sx

Hypereosinophilic Syndrome -

Persistent ^(6 months) eosinophilia $> 1500/mm^3$.
& end organ infiltration.

Known cause

1) PARASITIC INFESTATIONS
(Nematodes)

Loeffler's pneumonia

2) ABPA

3) Drugs:-

Nitrofurantoin

Sulfonamides

Isoniazid

Pencillamine

CHARACTER

Ac. EP

Ch. E. P.

Smoking H/o

+++ , new onset smokers

±

Asthma H/o

--

++

CF - Radiology

Acute shortness of Breath
+ Hypoxemia +
B/L diffuse infiltrates.

Cough + wheeze.
Peripheral opacities

Peripheral
eosinophilia

Initially not seen but seen
during later course of disease

usually seen

	AEP	CEP
BAL eosinophilia	BAL > 25% eosinophils	BAL > 40% eosinophils
Rx	steroid	steroid

ASPERGILLUS & LUNG

I> HYPERSENSITIVITY RxN. → DOC is steroid

Type I



Asthma

Type I, II, IV



ABPA

II> PNEUMONIA IN IMMUNOCOMPROMISED → DOC is VORICONAZOLE.
= Invasive Aspergillosis

Transbronchial angioinvasion. → may develop hemoptysis.
Fever + SOB.

DOC for I → STEROID.

DOC for II → VORICONAZOLE

III> COLONISATION IN PREEXISTING LUNG CAVITY

Aspergilloma / Fungus BALL

CXR → Air crescent sign.

→ Ball changing its position = deorbitus.



Rx - Resection if pt. is symptomatic

CRITERIA FOR ABPA

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- 1) Predisposing condⁿ -
 - Asthma
 - Cystic Fibrosis
- 2) Peripheral Eosinophilia
- 3) S-IgE \rightarrow $> 1000 \text{ IU}$
- 4) Aspergillus specific IgE + IgG will be +ve
- 5) Skin test +ve aspergillus fumigatus
- 6) CXR - fleeting opacities \rightarrow upper zone
- 7) Central (or) Proximal B' XIs.

Doc:- Systemic Steroids.

CT chest -

- Finger in Glove
- Toothpaste

HYPERSENSITIVITY PNEUMONITIS or Extrinsic Allergic Alveolitis

Type III + IV HSN

S-IgE \rightarrow (N)

No. peripheral eosinophilia

BIOPSY \rightarrow non caseating granuloma + cellular bronchiolitis +
Interstitial inflammation.

e.g.

DISEASE	EXPOSURE	ANTIGEN
1) Farmer's Lung	Moldy hay	Microsporypha fenig
2) Bagassosis	Sugarcane dust	Thermoactinomyces sacchari
3) Bird fancier Lung	Pigeon excreta	Avion protein Thermoactinomyces
4) Malt worker Lung	Mouldy Barley	Asp. clavatus
5) Hot tub lung	Contaminated water	Non-Tubercular mycobacterium

Δstic CRITERIA :-

- 1> Exposure to known antigens
- 2> Presence of serum precipitins against offending Ag.
- 3> Occurrence of symptoms in 4-6 hrs of exposure
- 4> Recurrence of symptoms on exposure
- 5> Inspiratory crepitation.
- 6> wt. loss

TYPES

ACUTE - hours to days

SUBACUTE - week.

CHRONIC - Month

C.T. Chest

Ground glass opacities

Centrilobular nodules

Fibrosis (upper zone)

Rx - Most Important → Avoidance of allergen.
Systemic steroids

ILD

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Defⁿ:- Group of Disorders characterised by predominant involvement of interstitium progressing to fibrosis & vary in mechanism & magnitude.

ETIOLOGY:-

I> Inhalational ILD

Organic Dust

Hypersensitivity
Pneumonitis

Inorganic Dust

Silica
Asbestosis

II> Drugs/ Radiotherapy

Amiodarone

Methotrexate

Busulfan

III> Connective Tissue Disorder

Scleroderma

RA

SLE

IV> IBDs

V> Infection - TB

VI> Malignancy

VII> Sarcoidosis

VIII> Idiopathic

PATHOLOGICAL PATTERNS:-

I> Usual Interstitial Pneumonia (UIP)

2> Non-specific " " (NSIP)

3> Acute Interstitial Pneumonia (AIP)

- 4) Cryptogenic Organising pneumonia (COP)
- 5) Respiratory Bronchiolitis (RBILD)
- 6) Desquamate Interstitial Pneumonia (DIP)
- 7) Lymphocytic " " (LIP)

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IOC :: ~~CT~~ HRCT chest

Confirmatory Test :: Surgical Lung Biopsy

RADIOLOGIC PATTERNS

Reticular Pattern.



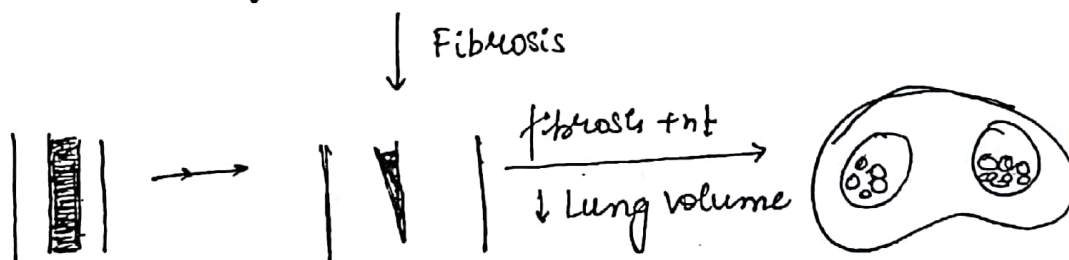
CT Chest



Mild opacity = Ground Glass opacity



↑ sed density = consolidation.



TRACTION
B³XIS

Honey combing
Subpleural involvement
(near to pleura)

M/C form

Usual Interstitial Pneumonia
or Idiopathic Pul. Fibrosis

C/F.

50-60 yrs $\sigma > \text{f}$, Smoker.

insidious,

Auscultation - Inspiratory crepts.
Exam - clubbing

Biopsy

Heterogeneous involvement
Fibroblastic foci

Radiology

- Bil Lower zone &
- subpleural involvement
- Minimal Ground glass opacity
- Significant Traction B'XIS
- Honeycombing

Rx + Prognosis

Poor response
to Predenidone
Nintedanib

NSAIP. (M/C form of
connective tissue
disorder associated
ILD)

40-50 yrs

$\text{f} > \sigma$

Non-smoker, subacute onset.

No fibroblastic foci

Lymphocytic inflammation

B/L ground glass opacities

Minimal Traction Bronchiectasis

Rare honeycombing

Good response to

steroid

ACUTE INTERSTITIAL PNEUMONIA/HAMMAR RICH SYNDROME

Pt - presents with acute SOB + Hypoxemia + Diffuse infiltrate
Idiopathic ARDS

Rx - supportive, High mortality

CRYPTOGENIC ORGANISING PNEUMONIA/ BRONCHIOLITIS

OBLITERANS ORGANISING PNEUMONIA (BOOP)

1) Pneumonia like illness

2) Proliferation of granulation tissue in airway \Rightarrow
MAISON BODIES

3) Presence of Interstitial infiltrate.

CXR:- B/L Peripheral Consolidation.

Rx:- STEROID.

SMOKING AND ILDs

Resp. Bronchiolitis associated ILD

Desquamate Interstitial Pneumonia

Adult Pulmonary Langerhans cell histiocytosis

Acute eosinophilic pneumonia

Pulmonary haemorrhage syndromes

Idiopathic pulmonary fibrosis

ILDs Less Prevalent In Smokers:-

1) Sarcoidosis

2) Hypersensitivity pneumonitis

SARCOIDOSIS

Multisystem Disorder characterised by non-caseating granuloma.

Etiology:- 1) Autoimmune

2) Propionibacterium

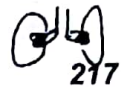
3) Mycobacterium

4) unknown.

5) Genetic susceptibility - HLA DRB, 1101

M/c → Pul. Involvement.

Scadding Staging I - Hilar adenopathy



II - " LNT + Lung infiltrates



III - Lung infiltrates alone



IV - Fibrosis



Upper Zone predominant Disease

PHENOTYPES

1) LUPUS PERINIO-

Cutaneous involvement → Bridge of nose
area beneath eyes + cheeks

2) LOFGREN SYNDROME-

Erythema nodosum, Hilar LNT
Uveitis (MC - Anterior), Arthritis

3) UVEO-PAROTID FEVER

Uveitis + Parotiditis + Fever + CN 7th Palsy

Δ:

1)



→ Release ACE. + $1,25(OH)_2 VITD$

Non-caseating
granuloma

↑ S. ACE > 2 times (N)

Hypercalcemia

2) Blood :- Peripheral Lymphopenia - sequestration of lymphocytes into lung

3) Bronchoscopy :-

BAL - Lymphocytes $\frac{CD4}{CD8} \uparrow$

4) Biopsy - Non-caseating granuloma

IOC → Incompatible clinical scenario → Biopsy of involved organ showing non-caseating granuloma is s/o Sarcoidosis

57 CT chest → Lung infiltrates
LN ↑

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In TB LN → Caseating → Central hypodensity + peripheral rim enhancement

Sarcoidosis → uniform density

67 Gallium scan

a7 ↑ uptake by Parotid & Lacrimal glands → ↑ uptake by mediastinal LN



"PANDA SIGN"



"LAMBDA SIGN"

Rx steroid + Immunosuppression.

↑. LEVELS OF ACE

- 1> Sarcoidosis
- 2> Leprosy
- 3> Gaucher's Disease
- 4> Hyperthyroidism
- 5> Disseminated granulomatous infect such as
- 6> miliary TB

Pneumonic. [Sar Le Ga DM ~~Hyper~~ thyro wale]

RA

M/c pulmonary manifestation
→ pleuritis

Low Glucose Pleural Effusion

ILD → NSIP, B^xIS

Rheumatoid ~~Arthritis~~ nodules

CAPLAN's Syndrome. [RA +
Pneumoconiosis]

[silica expo, coal expo]

SLE

M/c pul. manifestation = Pleuritis

Acute lupus pneumonitis.

⇒ Pulmonary capillaritis +
Diffuse alveolar H^ge

ILD → NSIP.

Shrinking Lung Syndrome



Diaphragmatic
involvement in
SLE.

SCLERODERMA

HIDE BOUND CHEST.

ILD NSIP → UIP, Pul. HTN

Mcc of death in scleroderma → Pulmonary cause

POLYMYOSITIS

↑ Anti JO1 ABS (

→ Anti Synthetase Sx.

→ C/F - 1) Fever

2) Myositis.

3) ILD

4) Arthritis

5) Mechanic Hands

DIFFUSE ALVEOLAR H₂O₂ / Pul HEMOSIDEROSIS

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Idiopathic Pul. hemosiderosis

- 1) Intra alveolar bleed
- 2) Fe accumulation as hemosiderin in alveolar macrophages
- 3) Fe deficiency anaemia

Pul. RENAL SYNDROME

- 1) SLE.
- 2) Good Pasture Syndrome
- 3) Small vessel vasculitis
 - ↳ Wegener's granulomatosis
- 1) Necrotising granulomatous vasculitis
- 2) RPGN
- 3) necrotising involvement of
 - URT → Epistaxis, sinusitis
 - LRT → Cavities, Diff. Alv. H₂O₂

OCCUPATIONAL LUNG DISEASES

SILICOSIS

H/c occupational lung disease worldwide

< 2.5 μ = Dangerous particles

ASBESTOSIS

Occupation Ship building, Construct' workers

Particle ~ ~ curvy serpentine
>> straight amphibole
(carcinogenic)

FEATURES



- 1) Pleural Plaques
 - ↳ Most specific for asbestosis
 - 2) Fibrosis
- α duration + exposure

SILICOSIS

sand blasting, quarrying

crystalline silica
Amorphous silica
1) silicotic nodules



- 2) Merging of nodules / coal macules
progressive massive fibrosis

COAL-WORKERS

PNEUMOCONIOSIS

Coal miners
Anthracite Bituminous

- 1) ~~Anthracosis~~
1) Anthracite
- 2) Bituminous

1) Anthracosis

- 3) complicated COPD
- 4) ↑ COPD

3) Benign pleural effusion.

4) H/c malignancy associated \bar{c} it

↓

LUNG CANCER

Smoking + asbestosis.

⇒ synergistic

Most specific

↳ MESOTHELIOMA

Lower zone Disease

Round Atelectasies



Organised Pleff. around segment
↓

Localised atelectasis

↓

COMET TAIL appearance

3) Silico-TB:- Chronic exposure

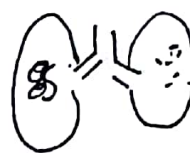
4) Alveolar proteinosis
↳ acute exposure

5) Malignancy.

CXR - Hilar LN + egg shell calcification

Upper zone Disease

5) Malignancy
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SLEEP APNOEA

Apnoea - Cessation of airflow for atleast 10 sec.

Hypopnoea - $>30\%$ reduction in airflow associated \bar{c}

$>3\%$ fall in SpO_2 .

SLEEP APNOEA

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CENTRAL

Resp. effort \ominus

Apnoea \oplus

Resp. drive \ominus

eg CHF
Narcotic Abuse

OBSTRUCTIVE

Apnoea \oplus

Persisting Resp. effort

\uparrow collapsibility of airway
at Neck.

R/F for obstructive Sleep Apnoea :-

- 1) obesity
- 2) $\odot \rightarrow$
- 3) Craniofacial Ab \odot
- 4) Hypothyroidism
- 5) Alcoholism

PATHOPHYSIOLOGY-

H/C Symptom \rightarrow Snoring.

APNOEA \rightarrow

HYPOXEMIA \rightarrow Pul. HTN, + Cor Pulmonale

\downarrow Arousal

\downarrow \uparrow Catecholamine Surge

$\swarrow \searrow$

CAD, MI,
arrhythmia,
Sudden cardiac death,
CVA.

\leftarrow \uparrow daytime Loss of quality
sleepiness of sleep
Loss of interest
Depression, Personality
changes.
RTA

Uncontrolled
HTN &

Poor glycemic control

Gold Std Δ :- Polysomnography

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- | | |
|---------------------|----------------------------------|
| 1) EEG | 6) Oronasal flow |
| 2) EOG | 7) Snore mic |
| 3) ECG | 8) Thorax + Abd. movement sensor |
| 4) EMG | a) Body position / Limb movement |
| 5) SpO ₂ | |

Other scales for assessment :-

- 1) Epworth sleepiness scale
- 2) STOP BANG Questionnaire

SEVERITY of OSA \Rightarrow APNOEA HYPOPNEA INDEX (AHI)

No. of Apnoea + Hypopnoea
Hour.

$< 5/h$ \Rightarrow (N)

$5-14/h$ \Rightarrow Mild OSA \rightarrow Behavioural Rx

$15-29/h$ \Rightarrow Mod. OSA

$\geq 30/h$ \Rightarrow Severe OSA

} Medical Rx of choice

CPAP - mild OSA +
comorbidities

In few cases \rightarrow Uvulo palatopharyngoplasty.

MALIGNANCY

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1° LUNG MALIGNANCY :-

Non-Small Cell Lung
Cancer
(NSCLC)

Small cell lung cancer
(SCLC)

- 1) Adeno Ca M/c worldwide
- 2) Sq. cell Carcinoma Mc in India
- 3) Large cell "

1) Small cell Ca /
Oat cell tumour.

LOCATION & ASSOCIATION OF TUMOURS:-

1) Central Location
&
Cigarette smoking

⇒ Sq. cell
&
Small cell (strongest association)
Endobronchial location.

2) Per:pheral Location
&
Less ~~m~~ smoking

Adeno Ca (♀, young ♂, less
&
Large cell
smoker)

3) Cavitation



Squamous
&
Large.

	ADENO	SQUAMOUS	SMALL CELL
Oncogene	KRAS / EGFR / ALK	FGFR, PI3K	myc, Bcl225
Biopsy	Glandular differentiation	Keratinisation + intercellular keratin bridges	Small round cell + hyperchromatic nuclei
Features	<p>→ Lepidic pattern</p> <p>Lung → Lung metastasis</p> <p>Scar Ca → Adeno ca</p> <p>(H/C Ca in asbestosis)</p> <p>↑ Clubbing → Hypertrophic osteoarthropathy</p> <p>Paraneoplastic</p> <p>↳ Hematologic</p>	<p>Central</p> <p>Cigarette</p> <p>Cavity</p> <p>Calcemia</p> <p>↑ paraneoplastic Life threatening</p> <p>↑ parathormone related peptid</p>	<p>ⓑ chemo + radio sensitive</p> <p>Rapid recurrence</p> <p>↑ metastasis</p> <p>↑ SVC obstruct</p> <p>POOR PROGNOSIS</p> <p>Clubbing is rare</p> <p>↑ Paraneoplastic Syndromes</p>

- 1) Hyponatremia - SIADH
- 2) Hypokalemia - Ectopic ACTH
- 3) Hypocalcemia - Calcitonin
- 4) Lambert Eaton Syndrome

CLINICAL MANIFESTATIONS of SCLC

5) Skin & Intercostal n/vs. → chest pain.

6) Pericarditis / Pericardial effusion.

7) Esophagus → dysphagia

8) Recurrent Laryngeal n/v → Hoarseness of voice

9) SVC obstruction.

10) Stellate Ganglion → HORNER'S Syndrome
(sympathetic ganglion)

Migratory thrombophlebitis
= Trousseau's Syndrome
+ clubbing = Adeno Ca

↓
Anhidrosis
Miosis
Ptosis
Loss of ciliospinal reflex
Enophthalmos

11) Distant Metastasis :- Brain / Bone / Liver.

H/c site → Brain

Most specific → Adrenals.

INVESTIGATIONS :

1) CYTOLOGY
 { Sputum
 { Pleural fluid
 } malignant cells

2) CXR - PA - Solitary Pulm. nodule
Collapse.
LN ↑
Pleural eff

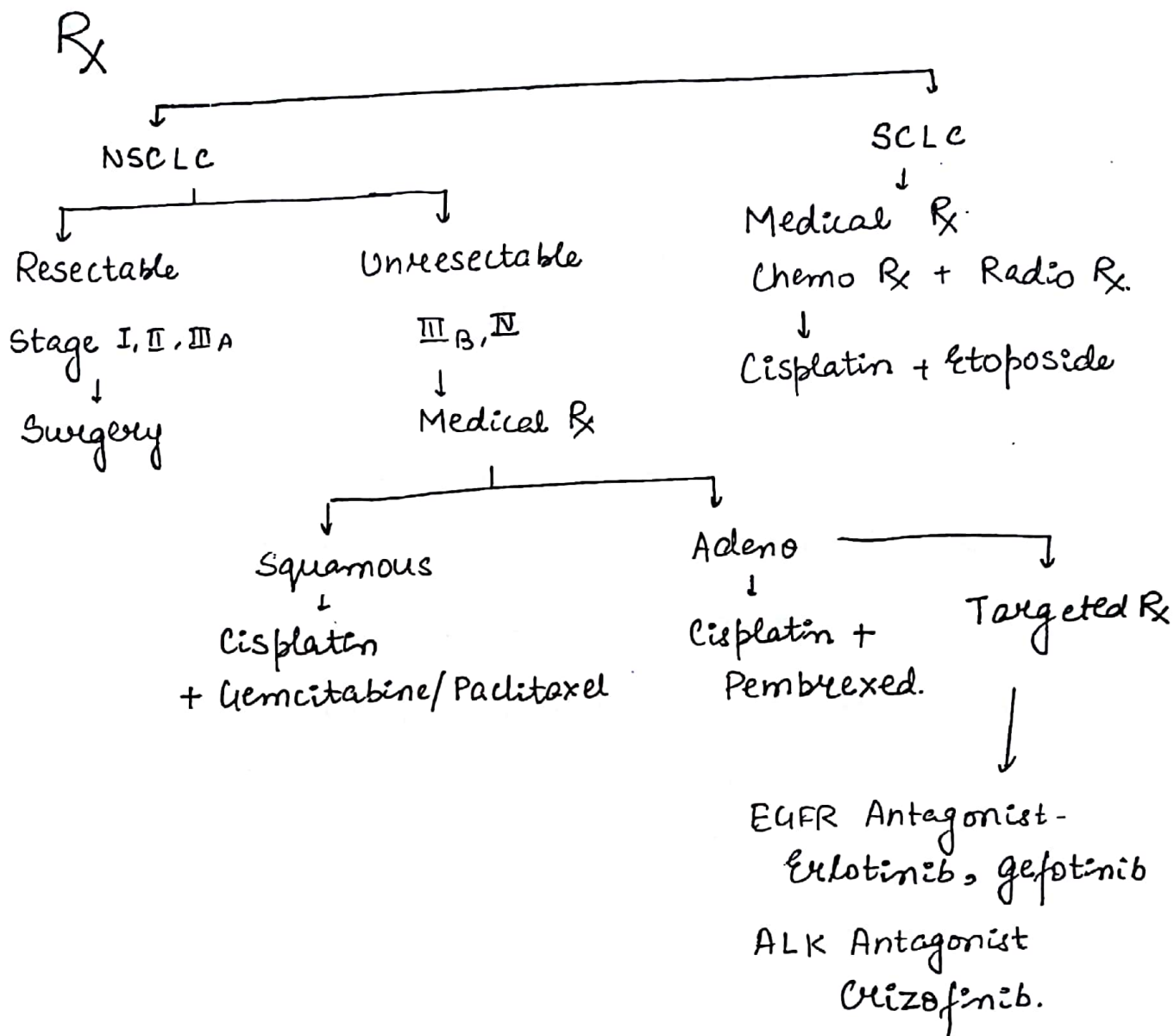
3) CT - Chest - Precise anatomical Location.

4) Gold Std → BIOPSY
 { CT guided
 { Bronchoscopy

5> PET SCAN - staging

6> Bone Scan

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Adeno Ca / ♀ / non-smoker / Asian ⇒ EGFR mutation.

Pancoast T_x - usually occurs in Sq cell
Located at apex.

May involve stellate ganglion.

PANCOAST SYNDROME = 1> Tumour in Lung Apex

2> Involve

→ 1st 2 ribs

→ stellate Ganglion.

→ C₈ T₁ T₂ → Pain, weakness in ulnar distribution

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Most Rapid method to identify of TB → Direct microscopy
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Most Rapid method for Rifampicin sensitivity = Gene
expert

PRESUMPTIVE TB

Any one of the following

Cough > 2 wks

Fever > 2 weeks

Hemoptysis

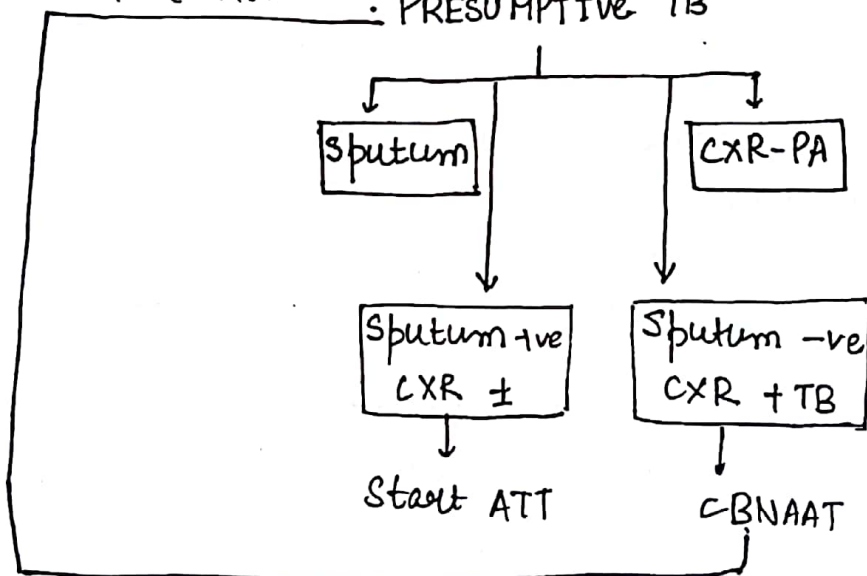
wt. loss

Abnormalities on CXR - PA view

ALGORITHM FOR Δ of TB

PT ± HIV

• PRESUMPTIVE TB



IGRA/Quantiferon Gold

Advantages:-

- 1> TB specific Ag → CFP & ESAT used
- 2> Less cross-reactivity ± BCG & NonTubercular mycobacterium
- 3> Blood Test
- 4> Serial Testing can be done ± out boosting phenomena
- 5> Single visit to hospital.

Disadvantage

Can't differentiate Infection vs Active disease

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PATHOLOGY

1° TB → unsensitised individual

2° TB → Post 1° TB → sensitised individual → Reinfection
Reactivation

1° TB

→ TB bacilli → mid + lower zone

→ Area of 1st contact

1° focus / Ghon's focus

→ Alveolar macrophage engulf TB bacilli

↓
⊖ Phagolysosome fusion

↓
↑ survival of M.tb

→ For immunity macrophages reach hilar LN → LN ↑

Ghon's complex → Ghon's focus + LN ↑

In LN →

↑ TH₁ response

* ↑ IFN-γ, TNFα

↓

↑ Killing capacity of macrophage

↓

Limit TB

Memory cells are formed



2° TB

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→ TB bacilli reach apex & actively grow.

→ Body's immune response will try to wall off infection.

→ After few weeks, Delayed Type HSN Response TB produced & destroys TB bacilli & Lung Parenchyma

2° TB is more infectious & it is active disease.

Calcified Ghon's Complex \Rightarrow Reinke's Complex.

TB/HIV

* If ART is started 1st \rightarrow ↑ Risk of immune Reconstitution. Inflammatory Syndrome (IRIS)

Start ATT 1st & merge ART in 2 weeks to 2 months

ATT = Always The Treatment

* If pt. is on TLE regimen. \rightarrow Rifampicin can be given

If pt. is on Nevirapine / Protease Inhibitor

↓
Rifampicin can't be given.
Rifabutin is given.

~~DISSET~~

DISSEMINATED TB

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CLASSICAL MILIARY TB	CRYPTIC MILIARY TB
1 ^o /2 ^o form	Elderly, chr. symptom
Hematogenous / Lymphogenous spread.	Fever, wt. loss, anaemia
Pathognomic. \Rightarrow Choroidal Tubercles	CXR - (N)
Sputum \rightarrow -ve	Sputum \rightarrow -ve
CXR - 1-2mm, Bil symmetric Homogeneous, millet shaped shadowing	Pt. collapses \Rightarrow death & autopsy reveals meningeal tubercles This is also miliary TB. but hidden on CXR.

NON-REACTIVE (or) AREACTIVE TB

Rare form

Acute Septicaemic form.

Underlying hematological abnormality

Fatal form

Autopsy shows areas of necrosis & out granuloma formation

R_x

New Case = 2HRZE + 4HRE = 6 months = DAILY

Previously R_x = 2HRZES + 1HRZE + 5HRE = 8 months = DAILY

HDR TB = Resistance to both H & R = DAILY

6-9 months \rightarrow E + Z + Kanamycin + Levoflox + Cycloserine + Ethionamide

18 months \rightarrow E + Levoflox + Cycloserine + Ethionamide

XDR-TB :- MDR-TB + Resistance to 1st 2nd line aminoglycosides
+ Resistance to 1 FQ

6-12 months - Capreomycin + Moxi + PAS + Clofazimine +
High dose INH + Amoxycylav + Linezolid

18 months - Moxi + PAS + Clofazimine + High Dose INH +
Amoxycylav + Linezolid

(24 - 30 months)

NEWER Anti-TB Drugs

BEDAQUILINE / Sirturo

2012

Diaaryl quinolone

MOA:- ATP synthase inhibition

S/E - QT Prolongation

DR TB.

Conditional access in India

Dose - 400mg
duration - 24 weeks.

DELAMANID

2014

Nitroimidazole

MOA:- Mycolic acid synthase
inhibitor

S/E - QT Prolongation

DR TB

Soon available in India

2

ACID, BASE, BALANCE & ABG

235

I) NORMAL VALUES

pH 7.35 - 7.45

pH $\leq 7.35 \Rightarrow$ Acidosis

Paco₂ 35 - 40 mmHg

pH $\geq 7.45 \Rightarrow$ Alkalosis

HCO₃⁻ 22 - 26 meq

(N) Paco₂ = 40

PaO₂ 70 - 100 mmHg

HCO₃⁻ = 26.

II) Relation Between pH, Paco₂ & HCO₃⁻

↳ Henderson Hasselbach Equation

$$pH = 6.1 + \log \frac{[HCO_3^-]}{Paco_2 \times 0.03} \Rightarrow pH \propto \frac{HCO_3^-}{Paco_2}$$

$$\downarrow pH \uparrow \propto \frac{HCO_3^- \uparrow}{Paco_2 \uparrow} \Rightarrow \frac{BASE}{ACID}$$

III) REGULATION OF pH Paco₂ & HCO₃⁻

Lungs $\uparrow \downarrow CO_2 \Rightarrow$ Resp. process

Kidneys $\uparrow \downarrow HCO_3^- \Rightarrow$ Met. process

SIMPLE ACID BASE DISORDER

1° process + Adequate compensatory response

Respiratory Acidosis

Resp. Alkalosis

pH \downarrow Paco₂ \uparrow HCO₃⁻ \uparrow

pH \uparrow Paco₂ \downarrow HCO₃⁻ \downarrow

Metabolic Acidosis

Metabolic alkalosis

pH \downarrow Paco₂ \downarrow HCO₃⁻ \downarrow

pH \uparrow Paco₂ \uparrow HCO₃⁻ \uparrow

In simple acid base disorder, always 1° change & compensation move together 236

In 1° resp. process → change in pH w.r.t. P_{aCO_2} & HCO_3^- in opposite direction

In 1° met. process — change in pH w.r.t. P_{aCO_2} & HCO_3^- in same direction

ROME

resp. opp, met. same direction.

Q. pH = 7.33, P_{aCO_2} 60, HCO_3^- 34
↓ ↑ ↑ ⇒ Resp. Acidosis
acidosis

Q. pH = 7.48, P_{aCO_2} 26, HCO_3^- 16
↑ ↓ ↓ ⇒ Resp. Alkalosis
alkalosis

Q. pH = 7.27, P_{aCO_2} 25, HCO_3^- 10
↓ ↓ ↓ ⇒ Met. Acidosis

Q. pH = 7.55, P_{aCO_2} 50, HCO_3^- 40
↑ ↑ ↑ ⇒ Met. Alkalosis

COMPENSATION

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Resp. Acidosis

Acute For every 10mmHg \uparrow P_{aCO_2} , $HCO_3^- \uparrow$ by 1 meq.

Chronic For every 10mmHg \uparrow P_{aCO_2} , $HCO_3^- \uparrow$ by 4 meq

Resp. Alkalosis

Acute For every 10mmHg \downarrow P_{aCO_2} , $HCO_3^- \downarrow$ by 2 meq

Chronic " " 10mmHg \downarrow P_{aCO_2} , $HCO_3^- \downarrow$ by 4 meq

Q Acute F.B. ingestion, pH = 7.32, P_{aCO_2} = 70, HCO_3^- = 29.

\downarrow

\downarrow

\uparrow

\uparrow

Acidosis

Acidosis.

40 $\xrightarrow{30}$ 70

26 $\xrightarrow{3}$ 29.

Resp. acidosis \bar{c} ~~complete~~ compensatory met. alkalosis.

Q Chr. neuromuscular disorder

pH = 7.34

P_{aCO_2} = 60

HCO_3^- = 34

\downarrow

\uparrow

\uparrow

chr resp. acidosis

40 $\xrightarrow{20}$ 60

26 $\xrightarrow{8}$ 34

Ans:- Chr. resp. acidosis \bar{c} compensatory met. alkalosis.

Chr. compensated Resp. Acidosis.

Metabolic Acidosis

Acute expected $Paco_2 = (1.5 \times HCO_3^-) + 8 \pm 2$. [winter's²³⁸ formula]

Q. $pH = 7.27$, $HCO_3^- = 10$, $Paco_2 = ?$

$$(1.5 \times 10) \pm 8 \pm 2$$

$$15 + 8 \pm 2$$

$$23 - 25 \Rightarrow \text{compensated}$$

Q. $pH = 7.26$, $Paco_2 = 18$, $HCO_3^- = 6$?

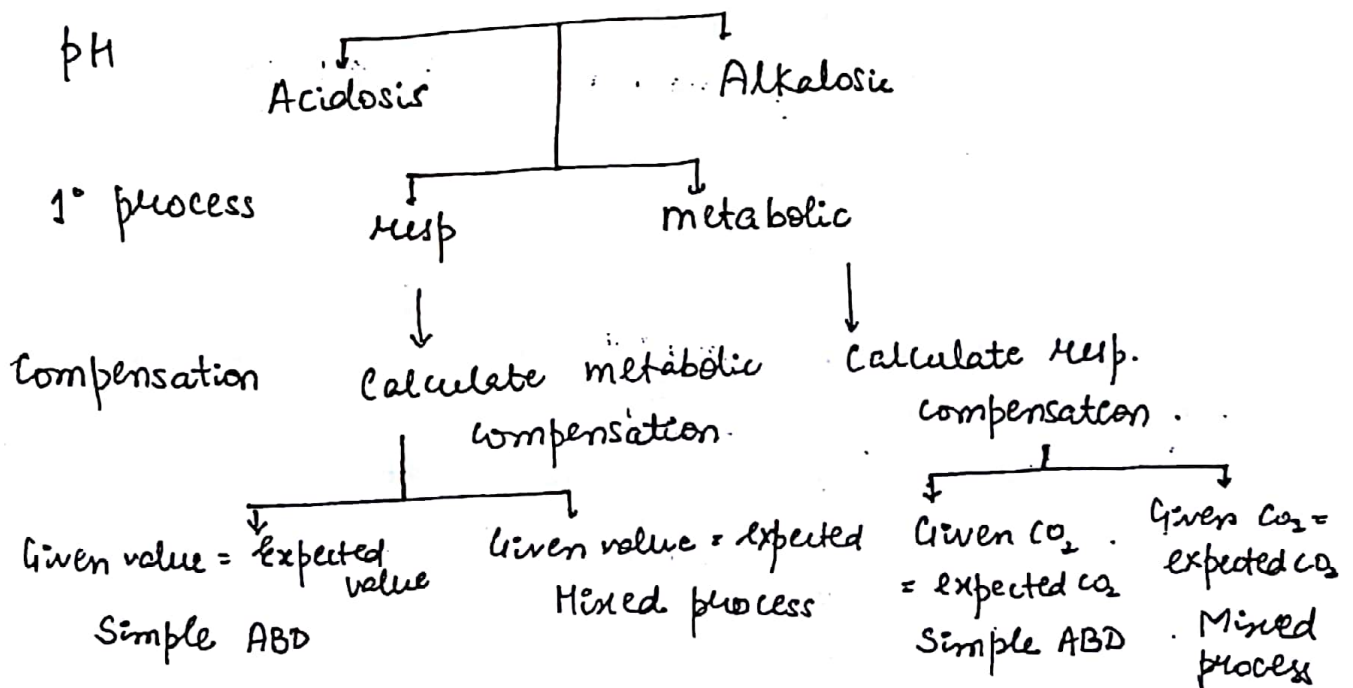
$$(1.5 \times 6) + 8 \pm 2 = 9 \pm 2 \quad \text{or} \quad 7 \pm 1$$

$$9 \pm 2 = 17 \pm 2 = 15 - 19$$

Met. acidosis \neq compensatory alkalosis

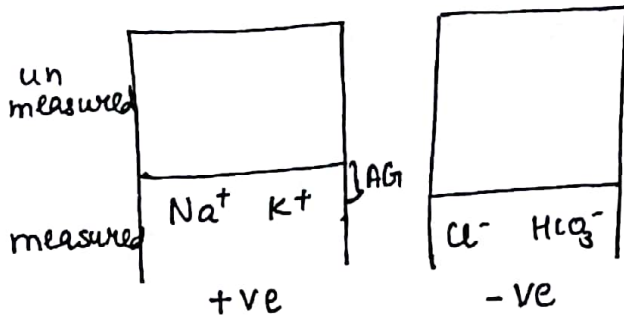
Metabolic Alkalosis

expected $Paco_2 = [HCO_3^- + 15]$



METABOLIC ACIDOSIS & CONCEPT OF ANION GAP

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$$(Na^+ + K^+) - (Cl^- + HCO_3^-) = \text{Anion Gap.}$$

$$(Na^+ + K^+) + \text{unmeasured cations} = (Cl^- + HCO_3^-) + \text{unmeasured anions}$$

$$(Na^+ + K^+) - (Cl^- + HCO_3^-) = \text{unmeasured anions} - \text{unmeasured cations}$$

$$[\text{Anion Gap}] = \text{unmeasured anions} - \text{unmeasured cations}$$

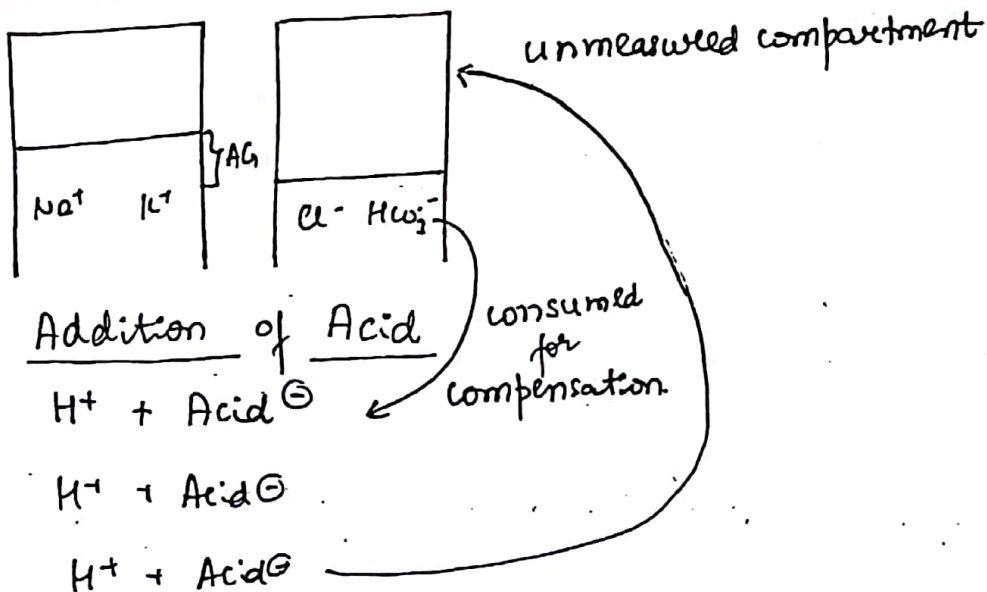
Common cause of ↑ in Anion Gap = ↑ in unmeasured anions

New Formula for Anion Gap

$$(Na^+) - (Cl^- + HCO_3^-) = AG$$

8-12 mEq.

HIGH AG METABOLIC ACIDOSIS



In pure High AG Metabolic Acidosis

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Rise in AG = fall in HCO_3^-

AG - 10 = 25 - Given carbonate.

$$\Delta \text{AG} = \Delta \text{HCO}_3^-$$

CAUSES :-

- I) TOXINS / DRUGS -
- 1) Methanol
 - 2) Paraldehyde
 - 3) Ethylene glycol / antifreeze
↳ oxalic acid
Oxaluria
 - 4) Salicylates

- II) Ketoacidosis - DKA
- 2) Alcoholic ketoacidosis
 - 3) Starvation

III) Renal Failure

IV) Lactic Acidosis

a) Type A Lactic Acidosis \Rightarrow [Hypoxemia]
[↓ perfusion]

eg. shock

Anaemia

CO poisoning

b) Type B Lactic Acidosis = [Perfusion: ⊕]

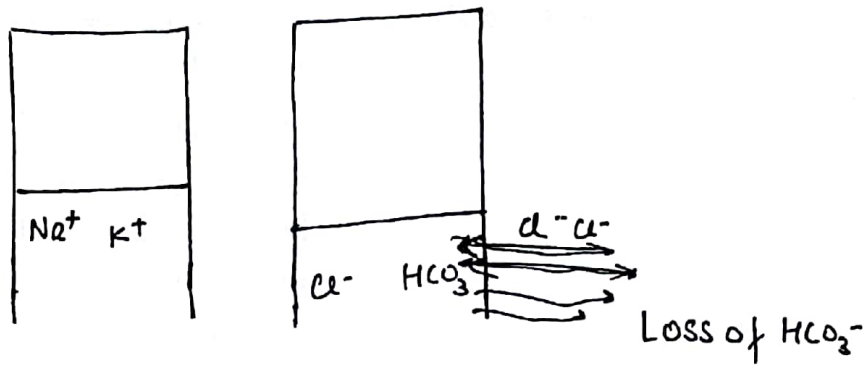
eg. Renal failure

Hepatic failure

Drugs - metformin
Zidovudine

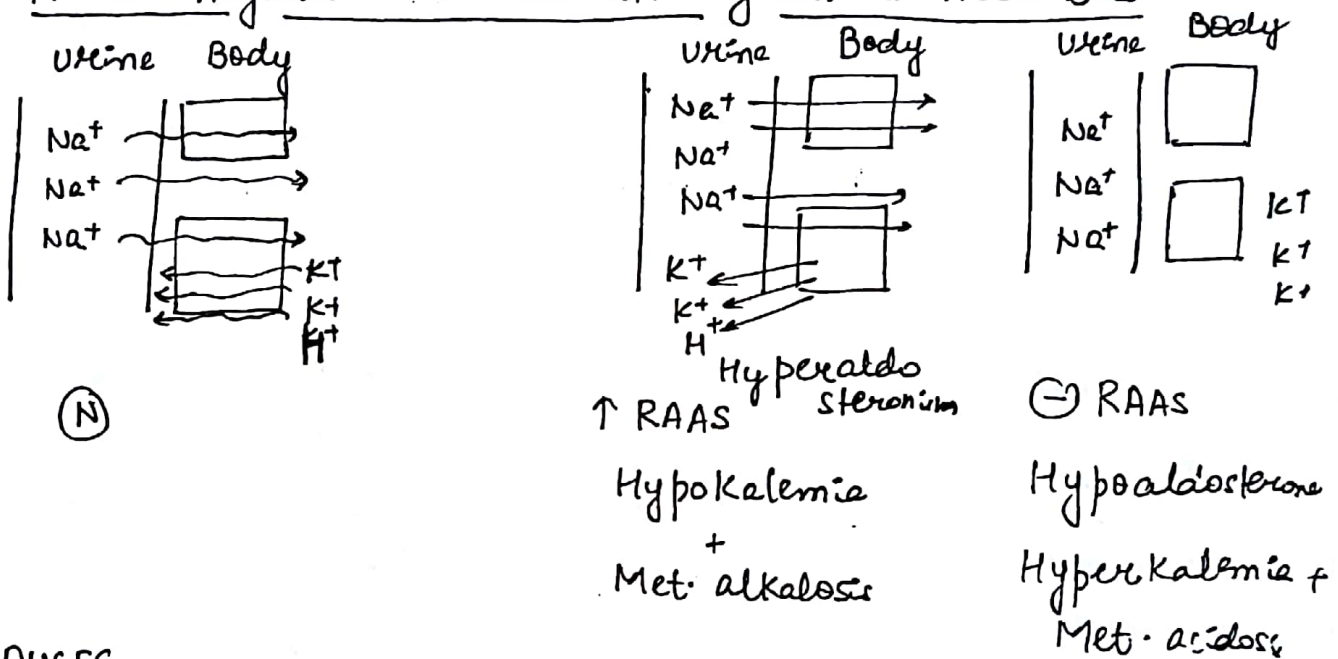
(N) AG METABOLIC ACIDOSIS

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Hyperchloremic Metabolic Acidosis

RENIN - Angiotensin - Aldosterone System in Acid. Base



CAUSES

I> GIT CAUSE

- 1) Diarrhea
- 2) Pancreatic fistula
- 3) Ureterosigmoidostomy
- 4) Enterocutaneous fistula

II> RENAL CAUSE

- 1) RTA
- 2) Drugs
 - ⓐ Carbonic anhydrase inhibitor
- ⓑ ACEI
- ⓒ ARB
- ⓓ Aldosterone antagonist

RTA

Type I RTA

Type II RTA

Met. acidosis + hypokalemia

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Type IV RTA

met. acidosis +
Hyperkalemia
(H/c type)

Causes

Hypokalemic state

Aldosterone resistance

" deficiency

Hypokalemic state

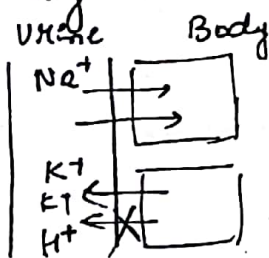
↳ Diabetic nephropathy

↳ chr. tubulointerstitial

Type I RTA

- Distal RTA

- H^+ excretion lost at
collecting duct.

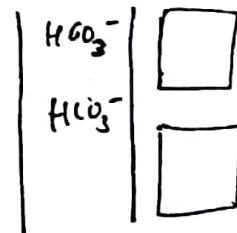


Met. acidosis
hypokalemia

Type II RTA

Proximal RTA

HCO_3^- reabsorption lost in
PCT



Bicarbonaturia can
induce kaliuresis
Met. acidosis +
hypokalemia

Urine anion Gap :-

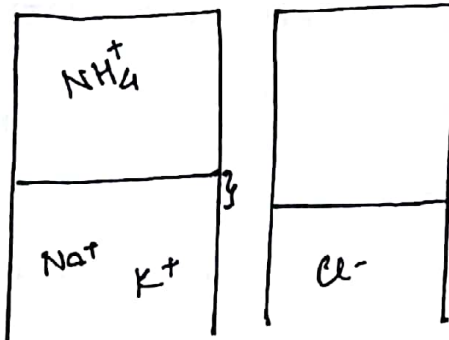
To differentiate (N) anion gap Met acidosis of diarrhoea²⁴³ v/s RTA

$$UAG = [Na^+ + K^+] - Cl^-$$

(N) value = 0-5.

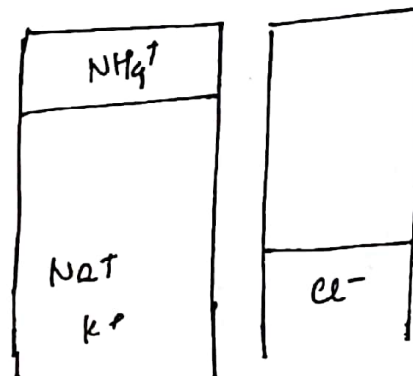
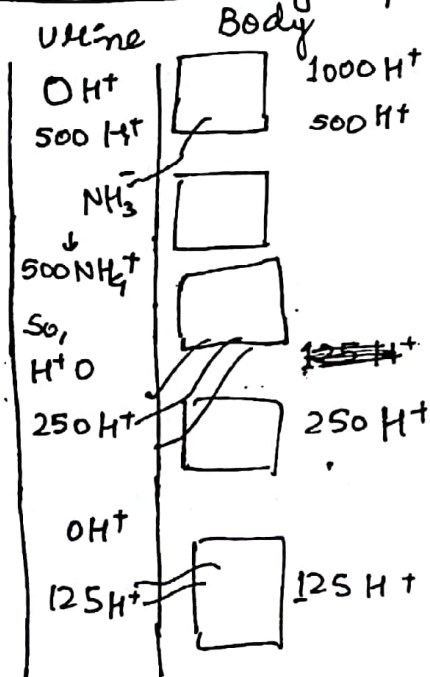


taking 0 as reference level



(N)

Renal Handling of Acid

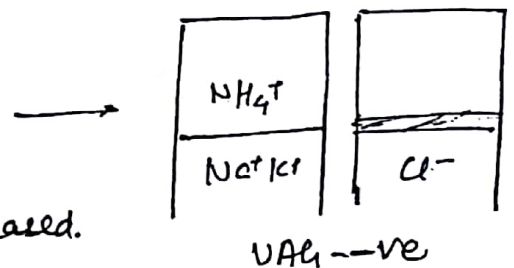


$$RTA = UAG +ve.$$

Diarrhoea :- Met. acidosis.

10,000 H⁺

Urinary NH₄⁺ is increased.



UAG --ve

RTA :-

UAG is indirect measure of urinary NH₄⁺ excretion.

UAG is negative in GIT cause diarrhoea
GIT

METABOLIC ALKALOSIS

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Initiating Event

1) ECFV contracⁿ, hypotension.

2) 1° mineralocorticoid excess → ECFV expanⁿ & HTN
(B) initiating + persisting event)

Persisting Event

2° Hyperaldosteronism

SALINE RESPONSIVE / Cl^- response

$\text{U}_{\text{Cl}^-} < 20 \text{ mEq}$

- 1) vomiting
- 2) Ryle's Tube aspiration
- 3) Diuretic use
- 4) Post hypercapnic Met. alkalosis

SALINE UNRESPONSIVE / Cl^- unresponsive

$\text{U}_{\text{Cl}^-} > 20 \text{ mEq}$

- 1) 1° Hyperaldosteronism
 - 2) Cushing's Syndrome
 - 3) Renin secreting Tumour
 - 4) Renal artery stenosis
 - 5) Liddle's Syndrome
 - 6) Bartter Syndrome
 - 7) Gitelman Syndrome
- HTN
- hypo to tension (B)

RESPIRATORY ACIDOSIS

Type 2 Resp. Failure

RESPIRATORY ALKALOSIS

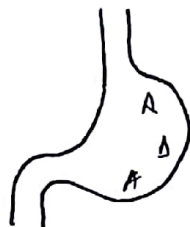
CHRONIC Resp. Alkalosis :-

M/c acid Base Ab(N) in critically ill pt

- 1) Pain, Panic, Psychogenic, Progesterone
⇒ Hyperventilation
- 2) Aspirin
a) vomiting → met. ~~acidosis~~ alkalosis

b) High AG metabolic acidosis.

→ When aspirin goes to blood



Resp. alkalosis.

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3) Theophylline

4) Fever, sepsis (change in sensitivity of Resp. centre)

5) CHF → Pul. oedema → stimulate of chemoreceptors

6) Cirrhosis of Liver → ↑ Glutamate

7) Severe ~~Hypotension~~ Hypoxemia → hyperventilation

8) ↑ ICP

ICU pts are also prone to Resp. alkalosis due to
pain, panic, psychogenic

Q. $\text{pH} = 7.32$, $\text{PaCO}_2 = 60$, $\text{HCO}_3^- : 34$.
 \downarrow \uparrow \uparrow = $\text{Chr. compensated Comp. Resp. Acidosis}$
 $40 \xrightarrow{20} 60$ $26 \xrightarrow{6} 34$

Q. $\text{pH} = 7.35$, $\text{PaCO}_2 = 60$, $\text{HCO}_3^- = 40$.
 \downarrow \uparrow \uparrow = Given value > Expected HCO_3^-
 Chr. Resp. acidosis + Add. metabolic alkalosis

Q. $\text{pH} = 7.28$, $\text{PaCO}_2 = 60$, $\text{HCO}_3^- = 26$.
 \downarrow \uparrow (N) Given value < Expected HCO_3^-
 Chr. Resp. acidosis + Add. metabolic acidosis

AG High AG or Normal AG.

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In pure High AGMA $\Delta AG = \Delta HCO_3^-$

Rise in AG = fall in HCO_3^-

$$[\text{Given AG} - 10] = [25 - \text{Given } HCO_3^-]$$

Q. Pt. is having DKA.

pts AG = 20

$HCO_3^- = 15$

$$\Delta AG = \frac{20 - 10}{10}$$

$$\Delta HCO_3^- = \frac{25 - 15}{10}$$

⇒ Pure HAG Met. Acidosis.

Q. Pt is DKA.

Pt. AG = 26

$HCO_3^- = 20$

$$\Delta AG = 10$$

$$\Delta HCO_3^- = 25 - 20 = 5$$

$\Delta AG > \Delta HCO_3^- \rightarrow$ Additional metabolic ~~acidosis~~ alkalosis

High
Additional AGMA + additional Met Alk

Q. DKA

AG = 20

$HCO_3^- = 10$

$$\Delta AG = \frac{20 - 10}{10}$$

$$\Delta HCO_3^- = \frac{25 - 10}{15}$$

$$\Delta AG < \Delta HCO_3^-$$

High AGMA + (N) AG metabolic acidosis

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If $\Delta AG > \Delta HCO_3^- \Rightarrow$ HAGMA + additional met. alkalosis

If $\Delta AG < \Delta HCO_3^- \Rightarrow$ HAGMA + additional met acidosis

Q. 14. 2014

20.

NEPHROLOGY

PHYSIOLOGY

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Kidney performs Diverse funcⁿ :-

- 1> Excretory :- urine formation
- 2> Homeostasis :- water & acid base balance
- 3> Hormonal :- erythropoietin synthesis & Vit D activation.

4> RENAL BLOOD FLOW

Kidneys are highly vascular.

Receives 25% of c. output

Even in presence of adverse condⁿ to the renal blood flow -

- 1> Dehydration
- 2> Hypotension
- 3> Renal artery stenosis

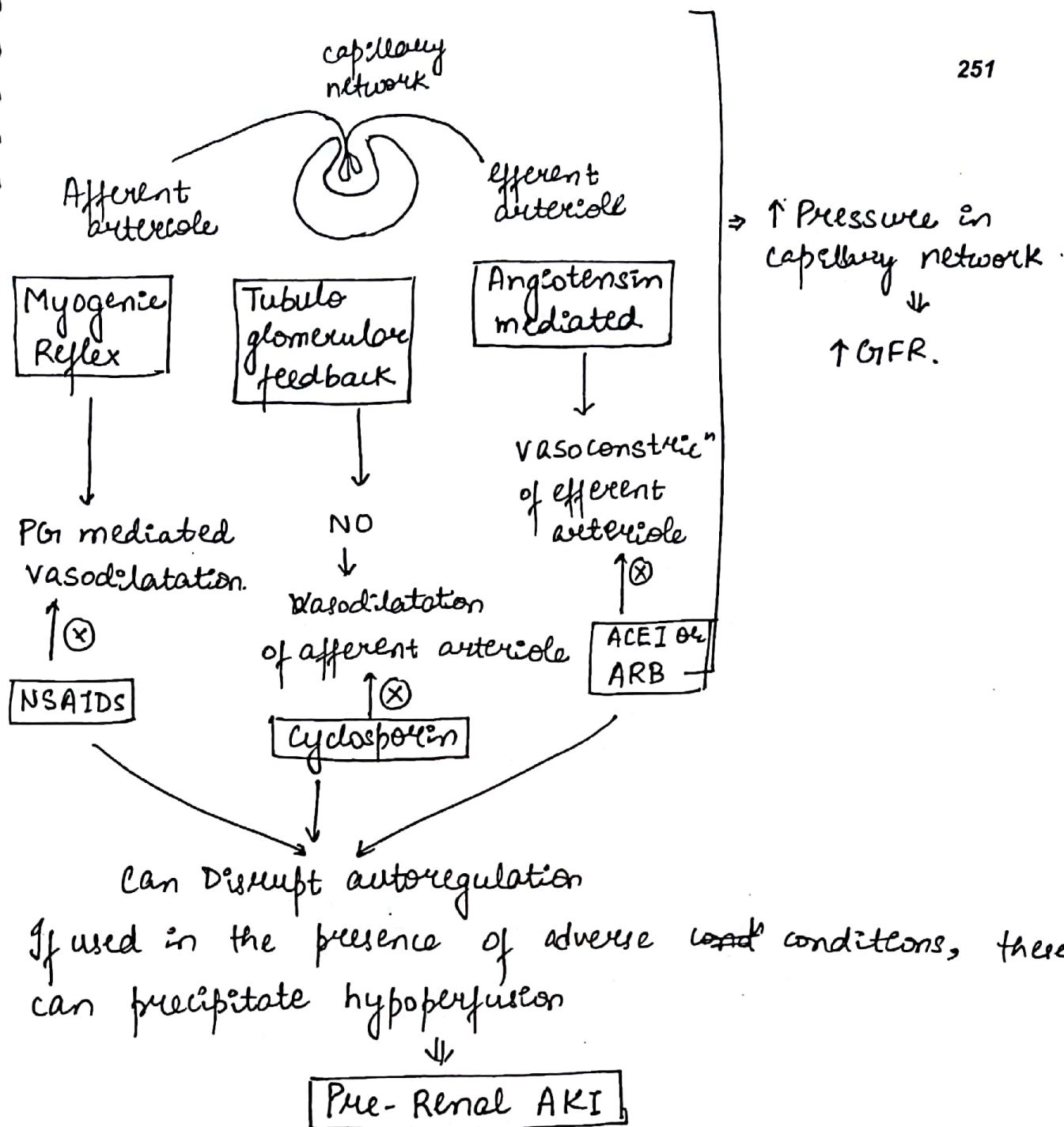
↓

Autoregulatory mechanisms activated.

⇓

Maintain adequate GFR.

- 1) ↑ Glomerular capillary Pressure



RENAL ARTERY STENOSIS

Cause → 1) 40% → atherosclerosis/arteriosclerosis
 2) 10% → FMD (fibromuscular Dysplasia)

Pathophysiology →

Activates RAAS

Vasoconstriction

Na⁺/H₂O retention.

M/C C/F → Sy. HTN

[M/C cause - 2° HTN - Renovascular]

ESG GUIDELINES - evaluation + Management

When to suspect/screen for R.A.S.?

- 1) young HTN (onset <30 yrs of age)
- 2) severe HTN <55 yrs of age (>160/110 mm of Hg)
- 3) HTN emergencies (sudden ↑ BP ± target organ damage)
- 4) Refractory HTN (uncontrolled ≥3, 1 is a diuretic)
- 5) Decline in GFR ≥30% after ACEI therapy (Disrupts autoregulation)
- 6) Asymmetrical kidneys on USG (Diff. ≥1.5 cm)
- 7) Unexplained Renal failure

Screening Tests

- 1) Duplex Doppler (Best)
 >98% sensitivity
 - Non-invasive, easy available
- 2) CT-Renal Angiography
 ↓
 C/I → GFR ≤ 60 mL/min
- 3) MR-Renal angiography
 C/I → GFR ≤ 30 mL/min
- 4) DTPA Scan (radio-isotope)
 (functional assessment of kidney)

Specific

- 1) Conventional Renal angiography
GRADING

% of Stenosis	Severity + Rx
<50% (Mild)	No further testing
50-70% (Moderate)	Follow-up
>70% (severe)	Always haemodynamically significant ↓ elective Rx

Rx 1st line → Medical
U/L B/L

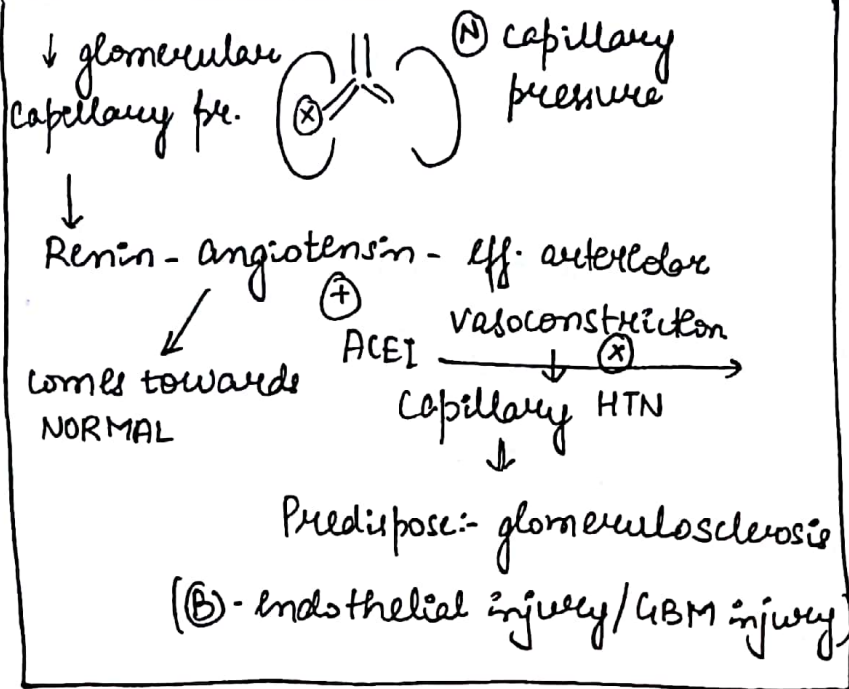
ACEI
(only drug =
protects (N) Kidney)

ACEI - C/I
CCB
β blocker
Diuretics

MOA of ACEI in U/L RAS.

Angioplasty 253

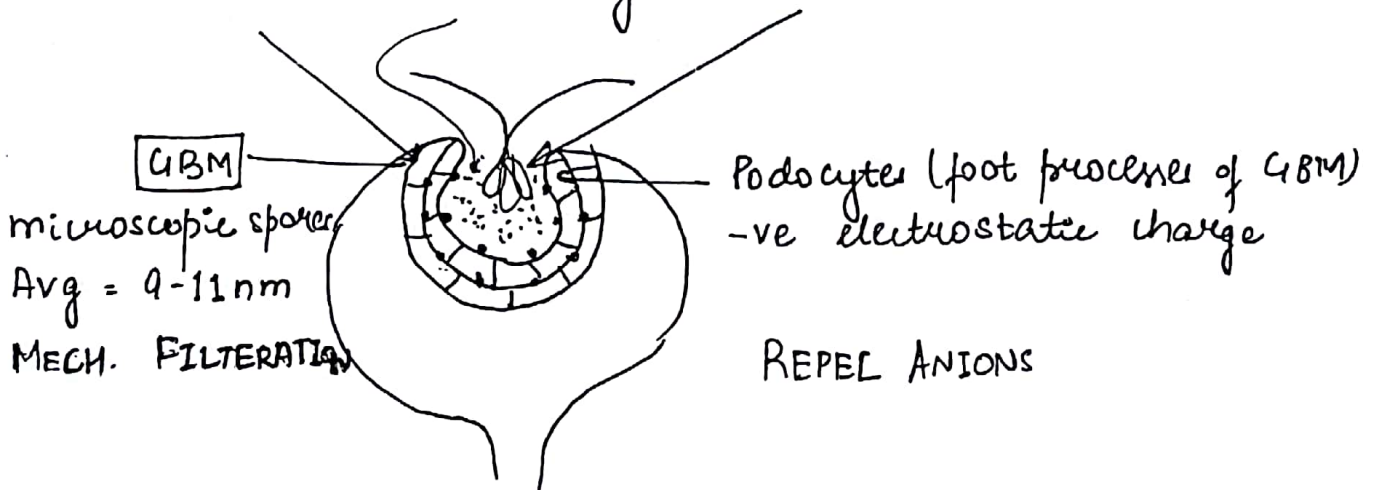
- 1) All - severe RAS
- 2) cause in FMD
(focal stenosis → so, easily Rx
= angioplasty)
- 3) Refractory Heart failure
(Flash Pulmonary Oedema)



Prognosis -
Favourable

URINE FORMATION

1st step → Ultrafiltration → Glomerulus
Intra-GBM ← Mesangium → outside GBM. (extra-GBM)



a) All Blood Components
RBCs, WBCs, platelets

① Albumin

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② Lipoproteins

b) All plasma proteins
(except albumin $\approx 4.6 \text{ nm}$)

③ AT-III, Protein S, C

GLOMERULONEPHRITIS

Predominantly affect GBM except Minimal Change Disease
(only podocytes affected)

- 1) Dysmorphic Hematuria (MPC)
- 2) RBC cast - Most specific
- 3) Non-selective proteinuria
- 4) Glomerular range proteinuria $[\geq 2 \text{ g/day} / 1.73 \text{ m}^2]$

- 1) NO HEMATURIA
- 2) Selective Proteinuria (albuminuria)
- 3) Dyslipidaemia
- 4) Hypercoagulable state

TUBULES

Reabsorption + secretion. (concentrating Ability)

Mechanisms:- Tubular transport

A) Cellular Transport
(across the cell)

B) Paracellular
(in betⁿ cells of tubule)

- 1) ACTIVE \rightarrow ATPase pumps.
- 2) PASSIVE \rightarrow exchange/co-transporters.

PCT
Leaky epithelia
 \downarrow
Allows BULKY Transport

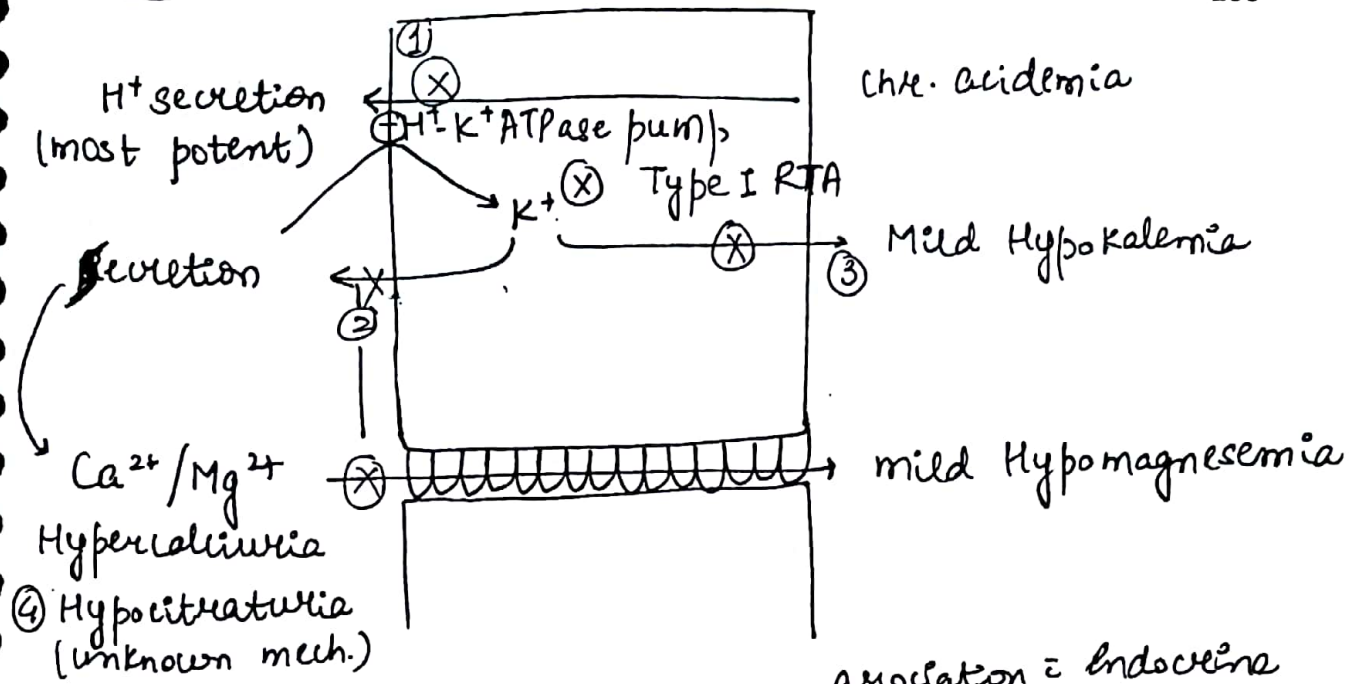
DCT
Tight Junctions
 \downarrow
Highly regulated

DCT

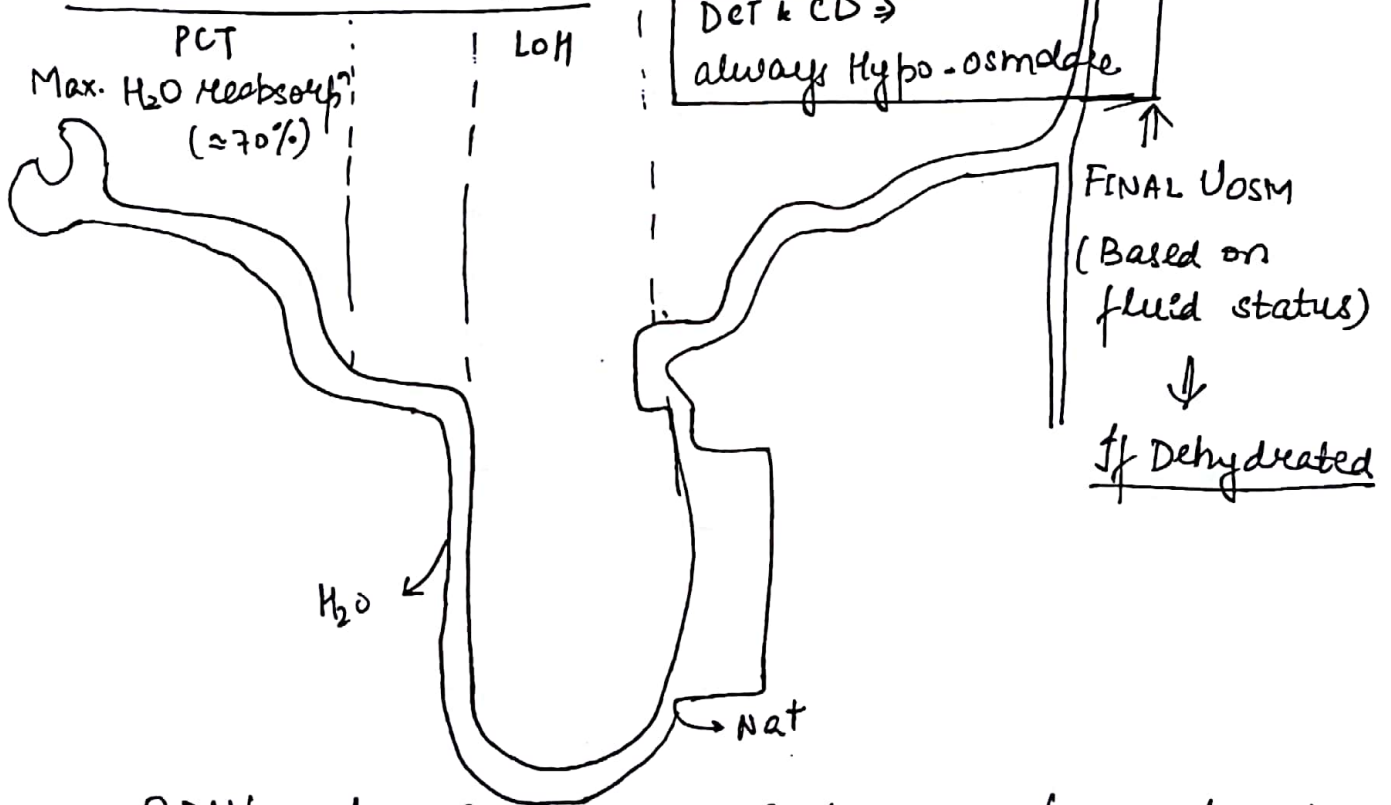
URINE

BODY

255



ROLE: WATER BALANCE



ADH (vasopressin)

V_2 receptors

AQUAPORIN channels

facilitate H_2O reabsorpⁿ

Restores plasma volume

Aldosterone (mineralocorticoid)

upregulates Na^+ channels

Na^+ reabsorpⁿ \downarrow secretes H^+K^+ exchange

Defⁿ:
Hypotonic Polyuria
(D. Insipidus)

Excess:-
oliguria (SIADH)

Defⁿ:
Addison's
(4C + MC Defⁿ)

Excess:-
CONN^{'s} ~~250~~
CUSHING's Syn.
↓
Hypokalemic
Alkalosis

HYPOKALEMIC ALKALOSIS

Due to aldosterone excess state

Causes:-> Endocrine (MC)

2> Chronic Drug use

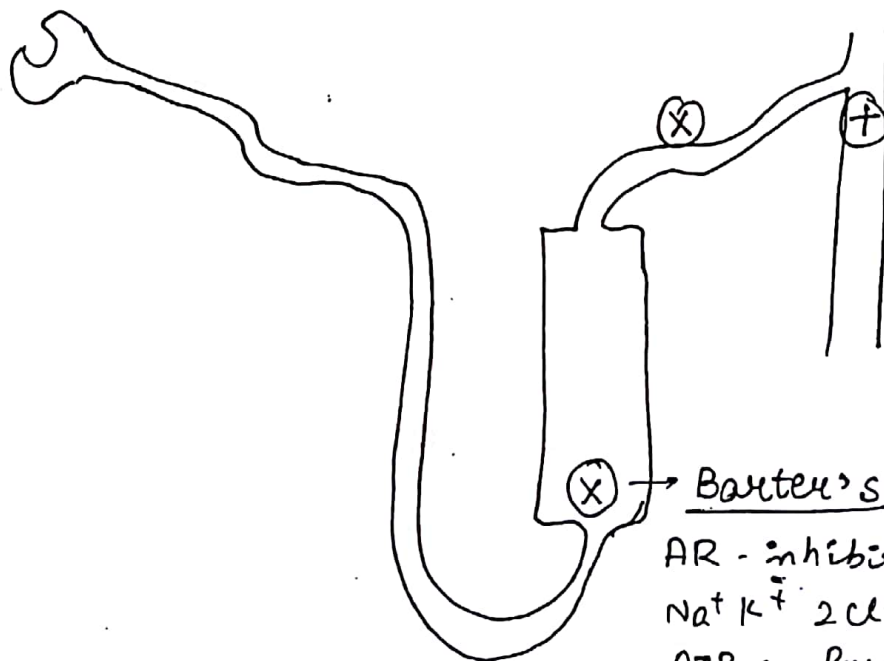
- Loop Diuretics
- Thiazides
- Steroids

3) Inherited Channelopathies

INHERITED CHANNELOPATHIES

Gitelman's Syndrome

AR inhibitory $\text{Na}^+ \text{Cl}^-$ cotransport
(Thiazide)



Liddle's Syndrome

AD - stimulatory
 $\text{eNa}^+ \text{c}$.

(Pseudo-hyperaldosteronism)
(steroids mimics this)

Bartter's Syndrome

AR - inhibitory
 $\text{Na}^+ \text{K}^+ 2\text{Cl}^-$

ATPase Pump

(Loop Diuretic)

Bartter's Syndrome (6 genetic mutⁿ)

Hitelman's Syndrome

LIDDLE's Syndrome 257

1) **Epid** → I.U.L → adolescence.
 2) **Patho** → $\text{Na}^+ - \text{K}^+ - 2\text{Cl}^-$ pump
 (X)(X)(X) - severe
 ↓
 1) (X)(X)(X) H_2O reabsorpⁿ

20-30 yrs

$\text{Na}^+ - \text{Cl}^-$ cotransport
 (X) Mild
 ↓
 (X) H_2O reabsorpⁿ

20-30 yrs

$\text{eNa}^+ \text{c}$
 (+) Mild
 ↓
 (+) H_2O reabsorpⁿ

3) **Plasma volume** ↓ ↓ ↓

↓

4) **B.P.** ↓ ↓ ↓

~~low~~ (N)

5) **Renin** ↑ ↑ ↑

↑

↑ ↓ ↓

Angiotensin

Aldosterone ↑ ↑ ↑

↑

↓ ↓ ↓

6) **Associated Defects** 30% - SNHL (Deaf)
 (unknown) mech & Paracellular
 (Ca) transport defect
 (Hypercalciuria)

Paracellular Mg^{2+} transport Defect

Pseudo-hyperaldosteronism.

7) **C/F** → 1) Polyhydramnios
 2) Failure to thrive
 3) Hypotension (syncope)
 4) Renal calculi

Muscle cramps
 Paralytic ileus
 Cardiac arrhythmias

'Asymptomatic Detection - HTN in young

8) **ABG analysis** ← Metabolic alkalosis. →

9) **S. K⁺** ← Low →

10) <u>Exclude chre. use</u>	Loop Diuretics	Thiazide	Steroids
11) Best Test S. Renin	↑↑↑	↑	↓↓↓
12) <u>Rx</u>	<div> <div>← HYDRATION →</div> <div>← K⁺ supplements →</div> </div>		
13) <u>Prognosis</u>	<u>Worst</u> (no cure)	Favourable	<u>AMILORIDE</u> <u>DOC</u> ENac antagonist - Safe in ☺ - Long term use - offers cure - BEST Prog
	<u>Trial of NSAIDS</u> as majority → ↑ PG. hence palliative (slow prognosis)	Mg ²⁺ supplements ↓ minimises symptoms	

ROLE OF KIDNEY IN ACID BASE BALANCE

Human Body → "Pro-~~acidic~~ acidic state"

Every living cell requires energy (ATP)

During ATP Production → Acid is generated.

(N) pH = 7.35 - 7.45 (slightly Basic)

MECHANISMS → ABB → Regulate pH efficiently

1) <u>Buffering</u>	<u>Resp mechanism</u>	<u>Renal Mechanism</u>
At tissue level HCO_3^- (extra cellular) ↓ $[\text{H}^+] + [\text{HCO}_3^-] \rightarrow \text{CO}_2 + \text{H}_2\text{O}$	<u>BACKUP</u> PO_4^{3-} (Intra cellular (Bones)) excretes acid in form of CO_2	Most Potent ↓ Acidification of Urine Most imp. form of H^+ secretion in urine → NH_4^+ ion. combines $\text{Cl}^- \rightarrow \text{NH}_4\text{Cl}$

$U_{H^+} \propto U_{Cl^-}$ levels.

HCO_3^- exhausted \leftarrow **ACIDEMIA** \textcircled{N} $U_{pH} = 6.5-7.0$ (Blood pH - \textcircled{N}) ²⁵⁹

PO_4^- required
Bone resorption
Rickets Osteomalacia

\Downarrow
Expected $U_{pH} < 5.5$ (Highly acidic)
 $U_{Cl^-} \uparrow \uparrow$
RTA
 \Rightarrow if kidneys are \textcircled{N}

\hookrightarrow Defect in acidification of urine
($U_{pH} > 5.5$, U_{Cl^-} - low in disease)

RTA

$\textcircled{2}$ HCO_3^- reabsorpⁿ
(also nutrient reabsorpⁿ)
 \textcircled{X} Type 2 RTA
(proximal RTA)

$\textcircled{3}$ HCO_3^- Regeneration
(Action - carbonic anhydrase)

\textcircled{X} Type 3 RTA
(Marble Brain Disease)

< 100 cases (worldwide)
 \hookrightarrow Majority:- cerebral calcification.
also - marble bone disease
(osteopetrosis)

Not included in routine classification.

$\textcircled{1}$ H^+ secretion

H^+-K^+ ATPase

\textcircled{X}
Type 1
(Distal RTA)

$\textcircled{4}$ Minor role
Aldosterone
 H^+/K^+ secretion.
in exchange of
 Na^+ + H_2O .

Type 4 RTA
(Hyper acidosis)

RTA	Type I	Type II	Type IV ^{M/C} RTA ₂₆₀
Epidemiology -	<10yr, M>F (Most severe)	20-30yr M=F (mild)	>50yr, M=F (Mildest)
	M/C inherited RTA		M/C RTA
Cause	Inherited	Inherited	Mildest (Acquired)
Association	30% autoimmune M/C - Sicca syndrome SLE (M/C Tissue) Mixed connective tissue Disorder	FANCONI'S syndrome - glycosuria - aminoaciduria Syndactyly	Early CKI. ACEI/ARB K ⁺ sparing diuretic Thiazide.
C/F	① short stature, Rickets ② Hypercalcaemia ↓ stone ↑ Renal calculi Nephrocalcinosis ③ Hypomagnesaemia ↓ M/s cramps	① mild acidemia Asymptomatic ② Vit D ₃ /PO ₄ def. (2° to loss in urine) ↓ Osteomalacia	① mild acidemia Asymptomatic ② Rarely Hyper K ⁺ complications
ABG analysis	← Metabolic Acidosis →		
Anion Gap	← (N) anion Gap →		
UAG	$(U_{Na^+} + U_{K^+}) - U_{Cl^-}$ [High/Positive]		
U _{pH}	always >5.5	maybe <5.5	always ⑤ <5.5

S. K^+

Low

(N)

High

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R_x

← Oral HCO_3^- supp. →

← Oral K^+ →

Citrate. supp.

↓ Renal calculi

(No cure)

Vit D₃/P₀₄ supplements

↓ Bone Disease

Stop offending drug
↳ offers cure

BEST.

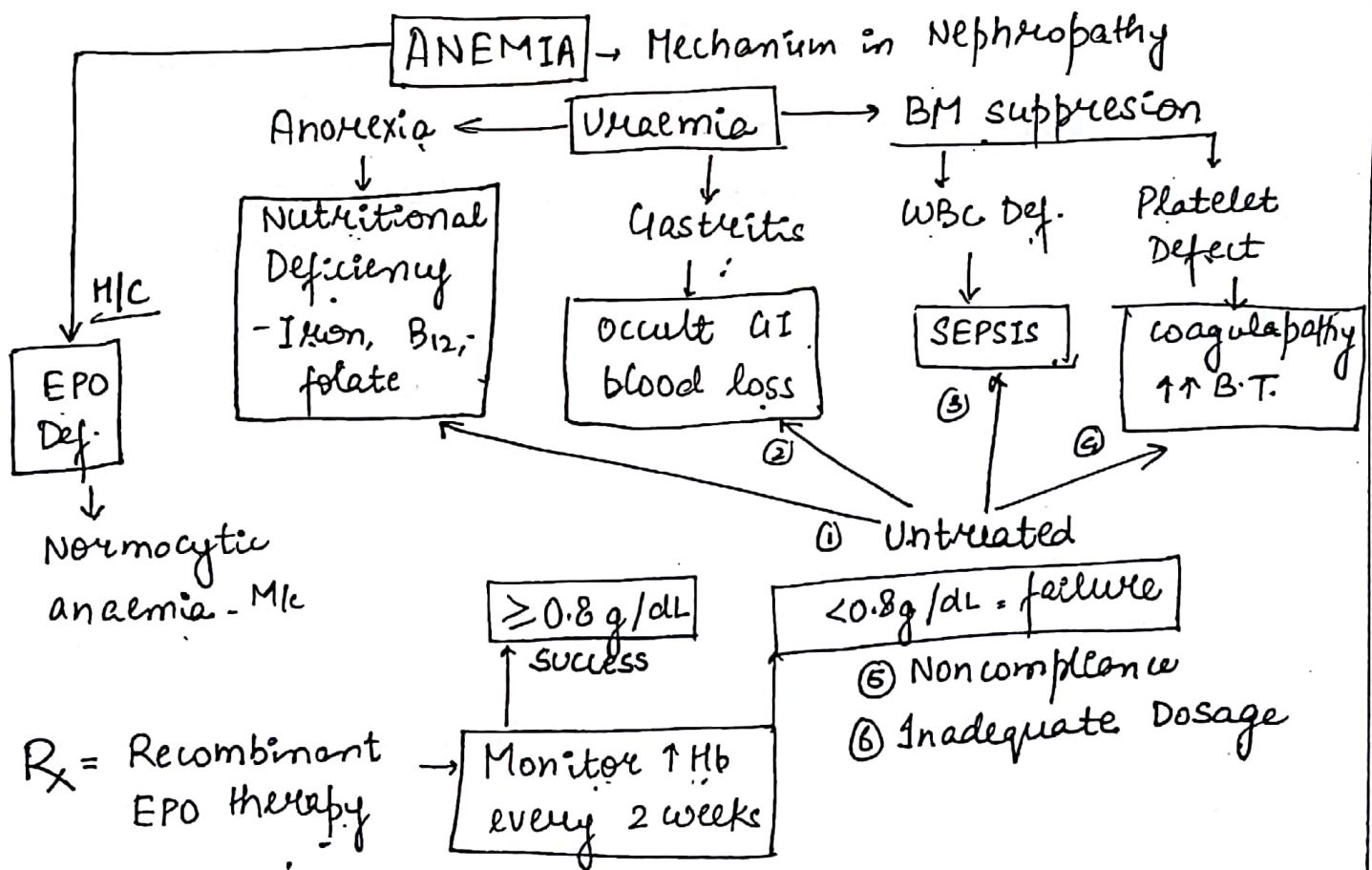
Prog.

WORST

Favourable

ANÆMIA

Defect in Erythropoietin Synthesis



Vit D → final step of activation into Vit D₃
& its reabsorption occurs in PCT

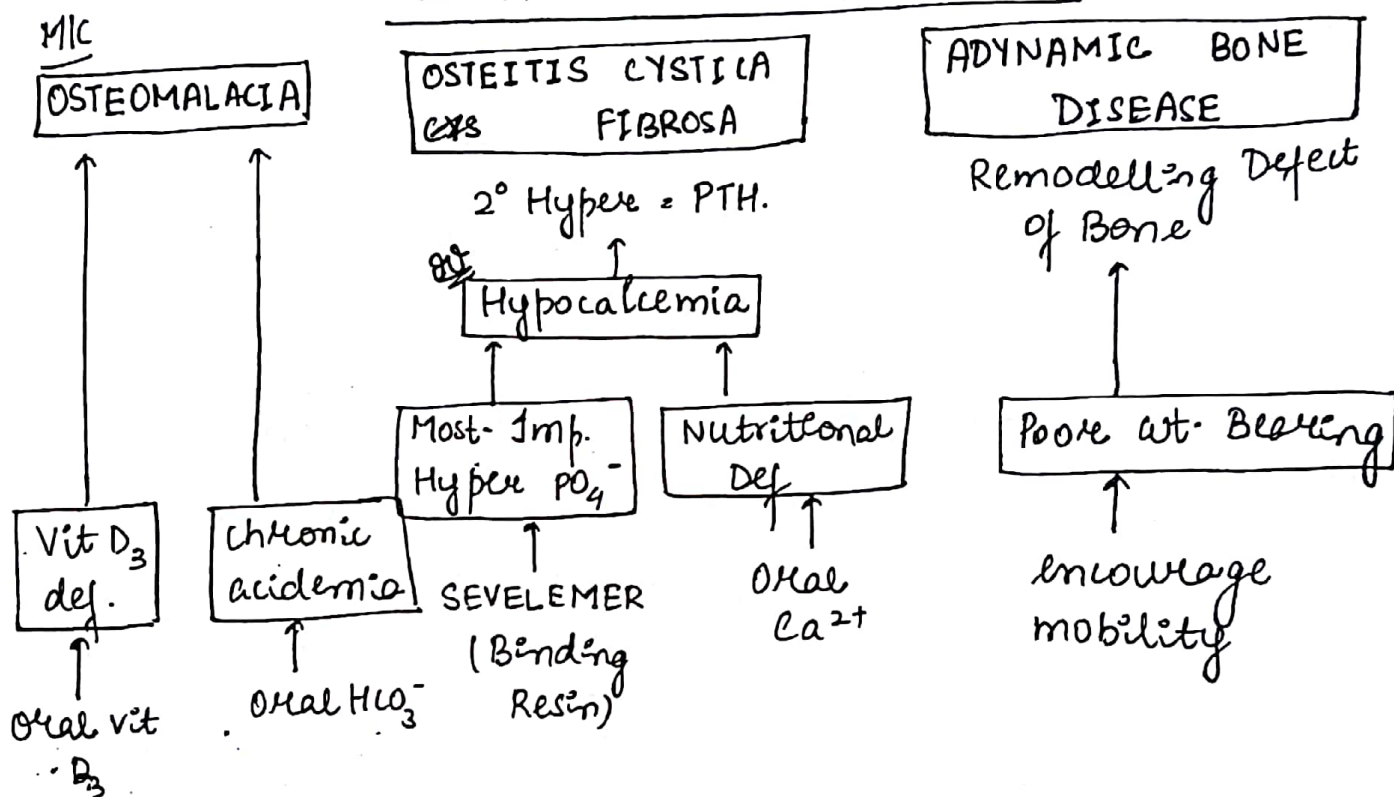
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↓ if Defective

BONE DISORDERS - in nephropathy

only C.K.I - Minimum (≥ 6 months) disease

RENAL OSTEODYSTROPHY



ASSESSMENT METHODS IN NEPHROLOGY

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S-CREATININE LEVELS (Best) screening Test)

C. PRODUCED

endogenously @ constant Rate
By Protein Breakdown.

EXCRETED

Freely filtered at glomerulus
Barely secreted/ reabsorbed @
tubules

S-Creatinine \propto GFR

↓ GFR

Renal Dysfunction

↑ S-Creatinine level

Early + sensitive
marker

Limitations of Test

- nonspecific for Δ of nephropathy.
- may not correlate immediate outcome of the disease
(Limited Prognostic value)

FALSE +ve ↑ S-Creatinine

↑ Production

a) High Protein Diet
b) strenuous exercise.
(athletes)

c) Infection (sepsis)

d) Inflammation (A.I.D.)

e) Neoplasms (some)

Alternative Test To S-Creat

S-CYSTATIN - C LEVELS

Produced endogenously
By all nucleated cells
@ constant Rate

Freely filtered @ glomerulus
Excretion \propto GFR.

Adv - not related to Diet or Exercise

NOVEL MARKERS OF AKI. = Specific for Δ of Nephropathy²⁶⁴

NGAL (neutrophil gelatinase associated Lipocalcin)

KIM-1 (Kidney Injury molecule)

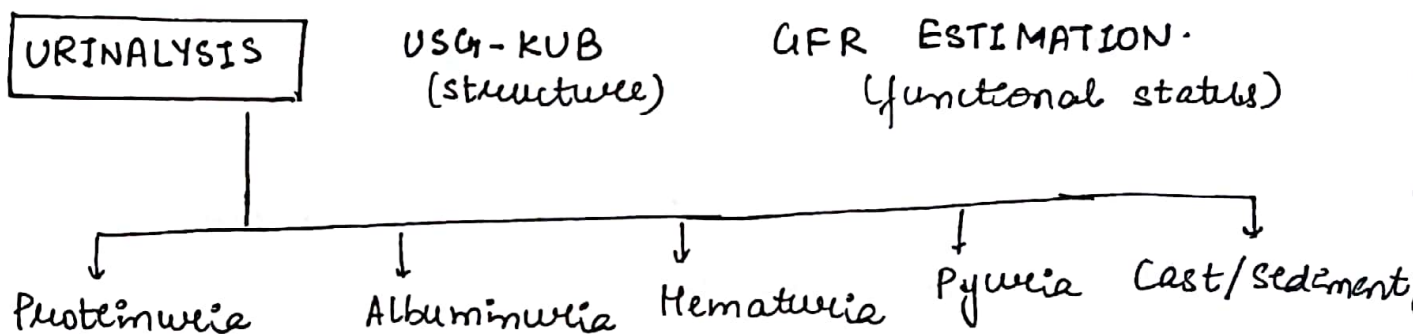
IL-18

Tested in spot urine sample^{or}

Are secreted by tubules in response to injury.

Hence detectable only in Renal causes of AKI.
(nephropathy)

TESTS - Detect :- SITE/CAUSE/SEVERITY



PROTEINURIA

Defⁿ - $>150 \text{ mg}/24 \text{ hours}$.

Detected using Dipstick Method
(very sensitive)

- Non-specific for Δ of Nephropathy
- Valuable in K/C/O - Nephropathy = identify SITE.
(Based on quantity)

$<2\text{g/day}$ (Tubular Range) ↓ Tubulointerstitial Disorders	$\geq 2\text{g/d}/1.73\text{m}^2$ (Glomerular Range Proteinuria)	
	$<3.5\text{g/d}$	$\geq 3.5\text{g/d}$
	Nephritic Range	Nephrotic Range

ALBUMINURIA

>30mg/24hrs

(More specific marker)

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QUANTITATIVE TESTS

Micro-alb

Cross-alb

24hr urinary alb.
estimation
(most reliable /
gold std)

30-300 mg of
Alb/24hrs

>300mg

(Most Preferred)
Spot urinary ACR
(alb/creat. ratio)

30-300 mg of
Alb/gm of creat

>300 mg

USE:- PROGNOSTIC

↓
Staging of CKI.

- Early marker
- Reversible stages
DOC = ACEI

Late / Irreversible
stages

Approach → HEMATURIA (RBC in urine)

Step 1 - Establish "SIGNIFICANT" (any+) | "INSIGNIFICANT"

- >3-100 RBC/hpf ≥ 3 occasions
- >100 RBC/hpf single occasion.
- GROSS HEMATURIA

only observation.
Repeat after 48hrs



Step 2 - urine microscopy : RBC morphology in urine

EUMORPHIC

Source - Below the
Renal Pelvis

Renal calculi
Cystitis
Carcinoma bladder



Radiological Testing

X-Ray
USG
CT



Inconclusive



Cystoscopy ± Biopsy

DYSMORPHIC (SOURCE → Renal Disease → GN)

GROSS H. Microscopic Hematuria

IgA nephropathy

Post-infective
Cause

Post-streptococcal
GN (PSGN)

Hep B - Polyarteritis
Nodosa

Hep C - Cryoglobulinemia
SABE

Lupus
Nephritis
(SLE)

OR

NORMAL

C₃ = initially Low
Returns to N - 6-8 wks

Persistently
Low
complement
levels

Approach - PYURIA (WBC in urine)

Step 1 : "SIGNIFICANT" > 5 WBC/hpf in centrifuged sample | observe/Repeat if not significant

Step 2 :- URINE CULTURE.

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M/c cause of significant pyuria = UTI.



STERILE PYURIA

CAUSES

Infective

M/c - Partially Rx UTI.

(> 72 hrs antibiotics)

FASTIDIOUS organisms

(special growth requirement)

Chlamydia

Mcc of STD

♀

Renal T.B.

Inflammatory

1) Renal Calculi

2) Papillary Necrosis

(severe tubular necrosis)

vascular insufficiency - Mech.

↓
DM - analgesic abuse

Sickle - Kawasaki Disease

3) Post - Radiotherapy

4) Post - Transplant Rejection.

Approach :- CASTS / SEDIMENTS

Common CASTS
But non-specific
for Diagnosis

M/c cast in urine

HYALINE CAST

Most Benign cast
NO further Rx / test

↑
M/c found in AKI.

M/c cast in nephropathy

GRANULAR / CELLULAR

Present in ⊕

Tubulo-interstitial GN

RARE CASTS
(10-15% cases)

RBC cast

WBC cast

Muddy Brown
Cast

Eosinophilic
Cast

Broad / waxy
Cast ↑
WORST CAST

DIAGNOSTIC

GN * (Acute GN)

Pyelonephritis

Acute Tubular Necrosis

Acute Interstitial Nephritis

C.K.I. *

Indicates total break
down of tubules.

USG-KUB

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(N)

Ab (N) & Its Interpretation

ECTOPIC → NO relation to function

1> SITE:- Anatomical

2> SIZE:- 7-11cms

<7cm (shrunken)

CKI (exceptions)

>11cms - Enlarged/Bulky

AKI. → classical in acute interstitial Nephritis

Early DM nephropathy

Adult PKD. (APKD)

HIV associated Nephropathy

Renal Amyloidosis

3> SYMMETRY <1.5cms

>1.5cms - asymmetrical kidneys.

Pathology → always in smaller kidneys

4> ECHOTEXTURE = (N)

Increased Echogenicity

↓
Active Disease in the Kidney

5> Cortico-Medullary Differentiation (CMD)

Most Imp. parameter

AKI

(Vs)

CKI

Preserved

Loss

6> COLLECTING SYSTEM - (N)

Obstructive uropathy

GFR ESTIMATION (Functional status)

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Most preferred = Creat. clearance
(Indirect/surrogate markers)
Easy, cheap, no radiation expo
Cockcroft Gault formulae
(estimated)

$$eGFR = \frac{[140 - \text{Age}] \times \text{wt. (kg)} (\sigma)}{72 \times S. \text{creat}}$$

$$- [] \times 0.85 \quad \text{♀}$$

Disad

- 1) Inaccurate (esp in AKI)
- 2) only - total Kidney GFR

Uses - MEDICAL

- 1) Staging of CKI
- 2) Follow-up - chronic medical Renal Disease
eg. DM, HTN, HIV associated Nephropathy
- 3) Dose adjustment of Nephrotoxic drug

Most Reliable/Gold std :-

Radio-isotope scan.
(DTPA, MAG-3)

Direct method.

Accurate

Single Kidney GFR

Segmental GFR.

Total Kidney GFR.

Disad

- Invasive
- Expensive
- Radiation exposure

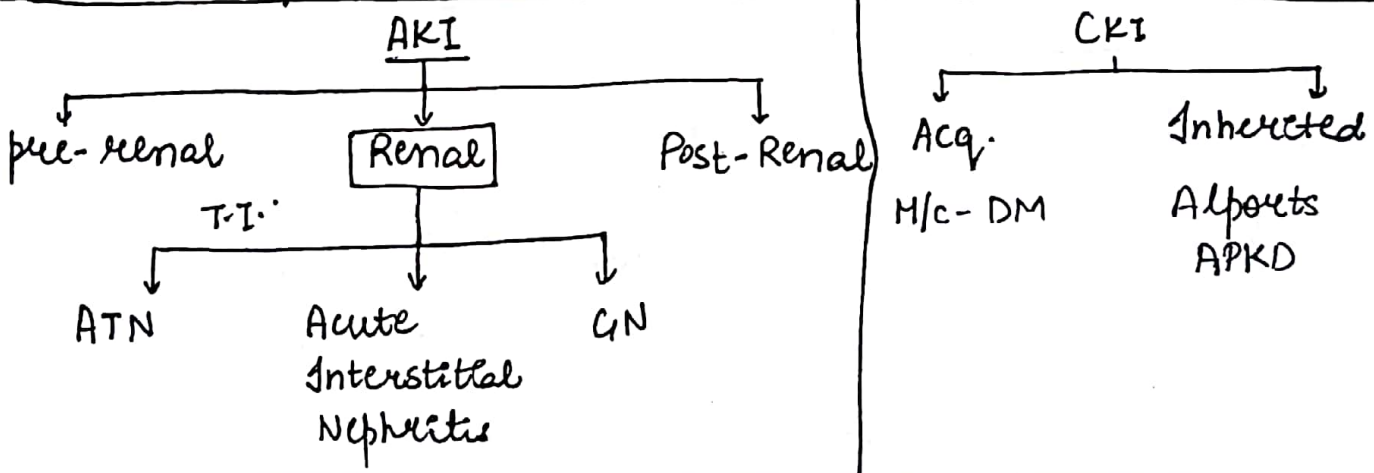
Uses

- Pre-Transplant assessment of DONOR
- Pre-op assessment of w/o sx
- medicolegal
- Decision making
↳ to operate on better kidney
never done B/L → risk of infection ↑

INDEX : RENAL DISORDERS

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<u>AKI</u>	<u>Parameters</u>	<u>CKI</u>
Preserved	USG = CMD	Lost
(N) or ↑	USG - size	(N) or ↓
Fluctuates - Posm	U osmolality	Isothenuria
Hyaline Cast	CASTS	Broad waxy Cast
⊖ uncommon	Anaemia	⊕ common.
uncommon.	Renal Osteodystrophy	⊕



R.R.T (Renal Replacement Therapy)

AKI

Defⁿ: Abrupt decline in GFR over short period²⁷¹ time

KDIGO Guidelines (Kidney disease improving Global outcome - part of National Kidney Foundⁿ)
Any 1

- \downarrow U.O. $\leq 0.5 \text{ mL/kg/hr}$ $\geq 6 \text{ hrs.}$ [oliguria].
- \uparrow S.Cr. $\geq 0.3 \text{ mg/dL}$ from Baseline $\leq 48 \text{ hrs}$
- \uparrow S.Cr. $\geq 1.5 \times$ Baseline $\leq 7 \text{ days.}$ (50% increase)

CAUSES OF AKI

Pre-renal

60-85% - HYPOPERFUSION

1) Dehydration

Diarrhoea
Hypoalbuminemia
Massive H²ge
Burns
(Insensitve losses through skin)

2) Hypotension

Cardiogenic
Septic shock.

3) Drugs - disrupt autoregulation.

Renal

INTRINSIC

45%

Tubulo
Interstitial
Disorder.

5%

GN

Post-renal

1-5% - OBSTRUCTIVE
UROPATHY

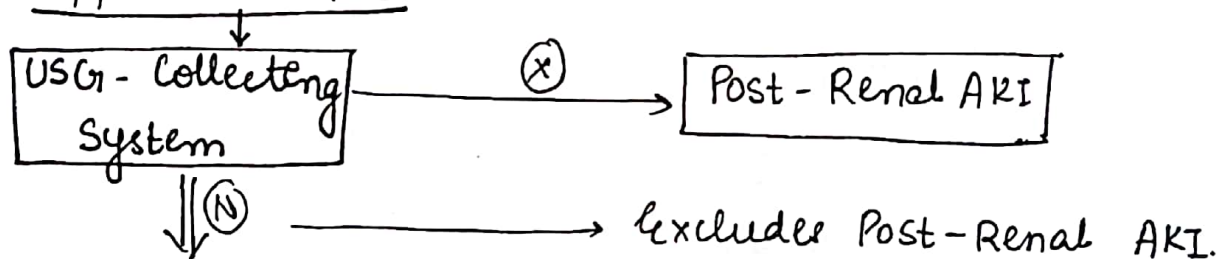
C/F	PR	Renal	Post-R
	<u>Classical 3 stages</u>	1) <u>Non-oliguric AKI</u>	Loin pain ²⁷²
oliguria <400mL/d		eg. SEPSIS	Dysuria
anuria <100mL/d		(In Tubulo-Interstitial)	Urgency
Diuretic phase (recovery)		2) Hematuria - GN	

Rarely - Serious UREMIC MANIFESTATIONS (cause - mortality in A.K.I.)

- 1) Encephalopathy / Convulsion
- 2) Pericarditis / shock
- 3) Coagulopathy

Ass → KDIGO Guidelines.

Approach - AKI



PARAMETER	PRE-RENAL	RENAL
MECHANISMS	RAAS ⊕ ↓ Na ⁺ /H ₂ O reabsorption ↑↑ Urate reabsorption.	Loss of concentrating ability Na ⁺ lost in urine Dilute urine
BUN : Creat	>20:1	<12:1.
U _{Na}	<20mEq	>40mEq
F _{ENa} ⁺	<1%	>2%

U _{osm}	> 500 mOsm/L	< 350 mOsm/L
CASTs	Hyaline casts	Granular/ ²⁷³ cellular
USG - Echotexture	(N)	↑ / Bright kidney
<u>Single Best</u> Novel markers of AKI	UNDETECTABLE	DETECTABLE

R_x PALLIATIVE

Indications of Dialysis

- 1) UREA > 100
 - 2) CREAT > 7
 - 3) SERIOUS UREMIC MANIFESTATIONS
 - 4) Refractory Pulmonary oedema
 - 5) Hyperkalemia > 6.5 mEq
 - 6) Refractory pH < 7.20
- Single most Imp. Indication for emergency Dialysis
- 7) Ingested Dialysable Toxin
- (commonly used: Accidental/suicidal)
- a) Salicylates
 - b) Methanol
 - c) Lithium
 - d) Polyethylene glycol (solvent)

SPECIFIC

Depends on cause

Ⓐ Post-Renal AKI

Early Sx relief
excellent recovery

Ⓑ Pre-Renal AKI

Fluid challenge (1st Line)
Inotropics

Antibiotics

Stop offending drug

excellent recovery

Delay in R_x → Progress to
ATN

Ⓒ RENAL AKI.

↓

Further evaluation.

95%

Approach - RENAL AKI

5%

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Tubulo. Interstitial	Parameters	CIN
<2g/day	PROTEINURIA	>2g/day
⊖	HEMATURIA	Common.
Granular	CASTS	RBC.

T. I. //

ATN	Parameters	Acute Interstitial Nephritis
>4%	FeNa ⁺	2-4%
Ⓝ	USG - size	enlarged / Bulky
Muddy Brown	CASTS	eosinophiluria

ATN (Tubule-M/c site)

Anatomy
Prone to
vascular
Insufficiency

Physiology
Site of concⁿ

Direct
Luminal
Contents

- 1) Untreated Pre-renal
- 2) sepsis
- 3) Contrast Induced Nephropathy
- 4) Drugs - aminoglycosides
- 5) Toxins - Heavy metal poison.
- 6) Cryoglobulinemia
- 7) Myoglobinuria
- 8) Hemoglobinuria

AIN

- 1) Allergic Response to Drug (M/c - 95% of case)
 - NSAIDs
 - Sulfonamides
 - Penicillin
 - Cephalosporin
 - Rifampicin
 - FQs
 - Dapsone
 - Nitrofurantoin
 - Contrast agents.
- ② Viral Infectⁿ
- ③ autoimmune
- ④ Lympho-proliferative

- Supportive therapy
- Underlying cause

Rx

4-6 wks

Arg. recovery

1-5%

Risk of ESKD

Favourable

Prognosis

Stop offending Drug-
Supportive Rx ²⁷⁵

1-2 wks

<1%

Good

GLOMERULONEPHRITIS

Causes :-

(A) PATHOLOGICAL :- Mesangial Involvement on Biopsy

(+) Proliferative GN

• Mesangio-proliferative GN
(IgA, PSGN)

• Crescentic GN (worst prog)
(RPGN)

• Membrano-~~capillary~~ proliferative GN
MPGN - mesangio-capillary

(-) Non-Proliferative GN

• Minimal Change Disease

• FSGN

• Membranous nephropathy

(B) CLINICAL PRESENTATION of GN (More Preferred)

Asymptomatic
proteinuria
microscopic
hematuria

(M/C)

Nephritic

- Hematuria
- HTN
- Rapid ↓ GFR.
(Risk - RPGN)
- Proteinuria
<3.5g/day

Nephrotic

- Anasarca
(Serous cavity)
- Hypercoagulable
State
- Preserved
GFR
- >3.5g/day
- $1.73 m^2$

Reno-vascular
HTN

C.K.I
eg. Alport's
Syndrome

Nephritic	Nephrotic
<ul style="list-style-type: none"> • PSGN • Lupus nephritis • RPGN 	<p>Children → MCD</p> <p>Adults → FSGS</p> <p>Elderly → membranous nephropathy (>50 yrs)</p>
↓	
Proliferative GN	Non-Proliferative
More likely nephritic	More likely nephrotic

MESANGIO-PROLIFERATIVE

	IgA nephropathy	PSGN
M/c cause	Worldwide	India
Epidemiology	20-30 yrs, ♂=♀	5-15 yrs. ♂=♀
Etiopath	← Post-infective	preceded by URTI →
Latent Period	< 1 st week Syn-pharyngitic	1-3 weeks 4-6 weeks ← SKIN
C/f	<p>Recurrent Gross Hematuria</p> <p>10-15% - Persistent microscopic</p> <p>Uncommon Benign nature of the disease</p> <p>S. IgA-I level ↑↑↑</p>	<p>Microscopic hematuria</p> <p>Common [classical nephritic syndrome]</p>
Screening (Serology)		<p>Anti DNA ase (70% cases +)</p> <p>ASO, anti-hyaluronidase</p>
Serum complement	(N)	Initially Low returns to (N) in 6-8 wks

HEMATURIA

HTN
↓ GFR

Biopsy	Mesangio-Proliferative changes	
Immunofluorescence	Granular Pattern of Ig deposits	
	Anti IgA staining	Anti IgG Staining
Rx	Reassurance Majority - self Limiting Risk of RPN $\leq 1\%$ Plasmaphereses	Penicillin - no role in nephropathy To eradicate residual Infection Long Term prophylaxis (X) Low relapse rates
Prognosis	BEST among GN	2nd Best (Risk of RPN 1-5%)

POOR PROGNOSTIC FACTORS

1) Elderly onset (> 40 yrs)

2) Nephrotic

3) Progression to **RP4N** - any GN requires RRT ≤ 1 month of onset

LUPUS NEPHRITIS

Kidney involvement - most dreaded.

organ involvement in SLE \rightarrow H/C of acute mortality

Deposition of Anti-dsDNA on GBM. (100% specific)

Type	PATHOLOGY	C/F	Rx
I	Minimal Mesangial proliferation.	Asympt - Proteinuria microscopic Hematuria Preserved GFR	No active Rx
II	Diffuse mesangial proliferation.		

III	Focal nephritis	Classical nephritis syndrome High risk - RPGN (15-20%)	I.v. methyl prednisolone therapy
IV	Diffuse nephritis		
V	MPGN/membranous	Nephrotic Synd.	oral steroids
VI	Glomerulosclerosis	CKI	Consider RRT

RPGN \rightleftharpoons Crescentic GN
(Clinical Asx) (Biopsy finding)

APPROACH - RPGN

Anti GBM Ab	ANCA	Serum. Complement levels	
<p><u>GOODPASTURE'S Syndrome</u> (GPS)</p> <p>Autoimmune</p> <p>20-40yrs $\sigma > \eta$</p> <p>α_3 subunit - Type 4 collagen</p> <p>↓</p> <p>Goodpasture's Ag</p>	<p><u>Vasculitis</u></p> <p>mimics GPS</p> <p>So, D/D. for</p> <p>Pulmonary-Renal Syndrome</p> <p>- Wegener's</p> <p>- Churg- Strauss</p>	<p>Low C_3</p> <p>↓</p> <p>Anti dsDNA</p> <p>Lupus (SLE)</p> <p>↓ ⊖</p> <p>Anti-DNAase</p>	<p>(N) C_3</p> <p>IgA</p> <p>Henoch-Schleiden Purpura</p>
<p>Alveolar BM GBM</p> <p>(Pulmonary Renal Syndrome)</p> <p>Alveolar H₂O₂ RPGN</p> <p>↓</p> <p>Mc among smokers</p>	<p>- microscopic polyangitis (MPA)</p>	<p>PSGN</p> <p>↓ ⊖</p> <p>HbsAg</p> <p>PAN</p> <p>HCV-Ab</p> <p>Cryoglobins</p> <p>↓</p> <p>ECHO:- SAGE</p>	<p>Plasma pheresis</p> <p>Poor Prog.</p>
<p>I.F.:- Linear pattern of Ig deposits</p>	<p>Sparse Ig deposits (pauci-immune)</p>		
<p>R_x ← PLASMAPHERESIS →</p>			
<p>Prognosis ← POOR > 70% acute mortality →</p>			

MPGN

Biopsy Based Δ sis
30-50 yrs.

♂ > ♀

90% causes → 2° causes

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70% cases → Low C₃ Level

causes

1> Infections - Leprosy
Malaria
Syphilis
Hep. B
Hep. C

2> Autoimmune - Type II ~~MPGN~~ Lupus
nephritis

3> Solid Organ Tumours - [H/c Renal manifestation = MPGN]

4> Lymphoproliferative states

C/F

Majority → "NEPHROTIC SYNDROME"

Asx

Renal Biopsy - Double BM/
Tham track appearance of GBM.

[Only INTRA-GBM MESANGIAL involvement]

↳ causes splitting of GBM.



10% Idiopathic → Rx - Immunosuppressants

FS GS (MC - adults)

1° (idio) MC Biopsy finding = sclerosing type of FSGS	2° Cause end point of DM HTN Reflux induced
Most severe <u>collapsing</u> type of FSGS	HIV associated nephropathy

C/F - HTN

Early & severe feature

Rx underlying disease +
strict HTN control

Risk of ESRD	Common - slow 15-20 yrs	
Acute mortality	No	Favourable Prognosis

MEMBRANOUS NEPHROPATHY (MC > 50 yrs) 280

85%

1° (idio) EM finding (Gold std) Spike & Dome appearance of GBM	2° cause Same as in MPGN
---	--------------------------------

NEPHROTIC

WORST Hypercoagulable
State

Hence, max. risk → RV Thrombosis

Anti-coagulation (all cases) +
Immunosuppressants

Common - 5-10 yrs	
Present (vascular)	WORST PROG.

C.K.I.

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Gradual \downarrow GFR ≥ 3 months duration.

Kidneys \rightarrow Large Functional Reserve.

Clinical Disease \geq 70% Loss of nephrons \approx 25-40 mL/min eGFR

CF -

17 UREMIC Symptoms (M/c) \rightarrow H/c neurological feature (90%)

- \rightarrow Encephalopathy / convulsions
- \rightarrow Pericarditis / shock
- \rightarrow Gastritis / Anorexia
- \rightarrow Infertility / Loss of Libido
- \rightarrow Proximal myopathy
- \rightarrow Peripheral neuropathy
- \rightarrow Restless Leg Syndrome
- \rightarrow Generalised pruritus

Peripheral neuropathy

- (axonal variant)
- Poor recovery inspite dialysis

27 FLUID OVERLOAD Symptoms
periorbital edema
peripheral "
CHF

37 Metabolic Acidosis

47 ANAEMIA - CKI

57 Renal Osteodystrophy

Asu - Done

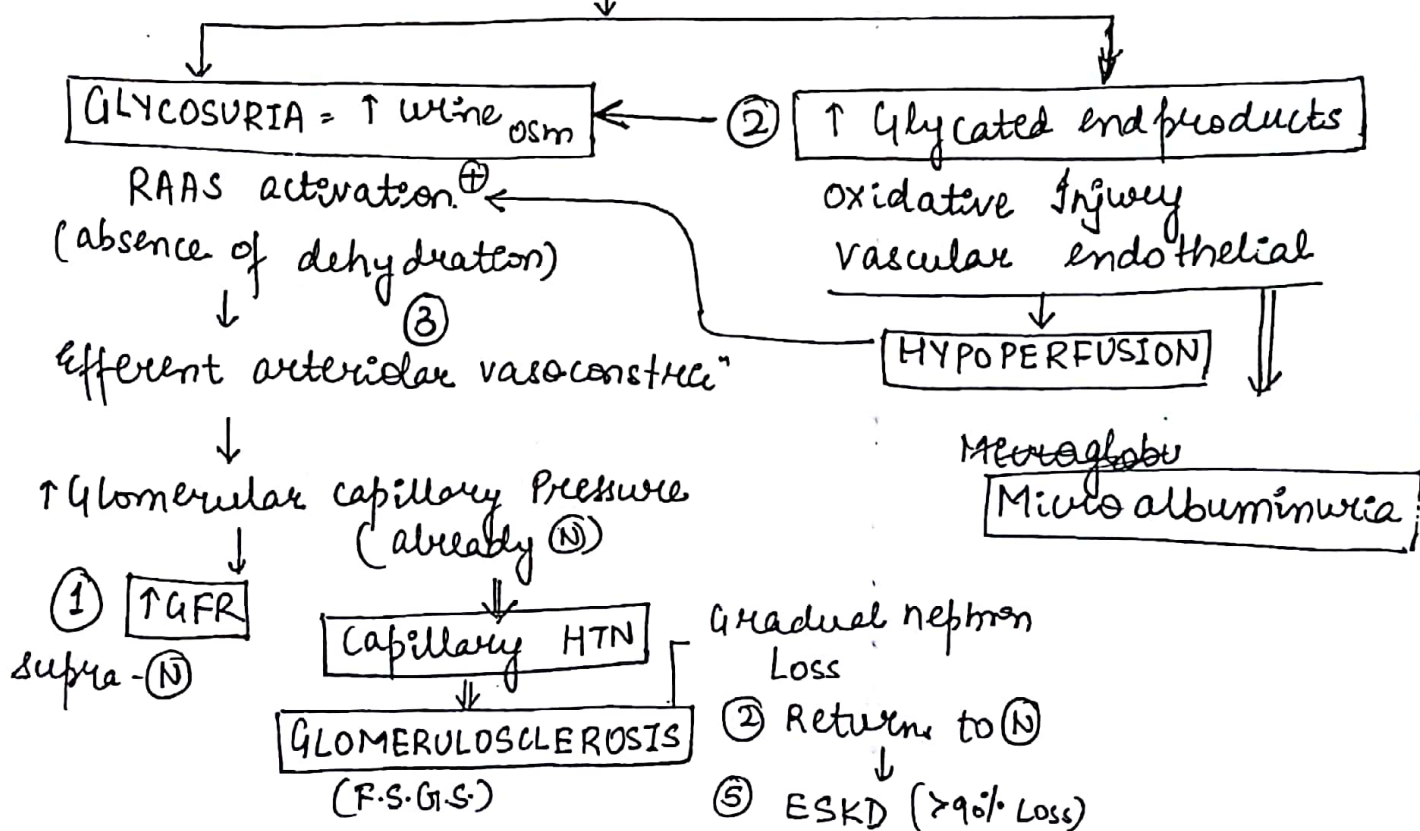
Rx	STAGE of CKI	2 Parameters		Rx
		Albuminuria	eGFR	
I } II }		Microalbuminuria (Reversible stage)	90-120 mL/min	ACEI + strict control of Risk factors (DM, HTN)
			60-89 mL/min	
III }	IV }	Gross (irreversible stages)	30-59 mL/min	Counsel + Prepare for RRT
V }			15-29 mL/min	
ESRD		Gross	<15 mL/min (→ 90% nephron Loss)	RRT is mand- atory

Specific Rx - Depends on Cause.
 { DM
 { alports
 { APIKD

DIABETIC NEPHROPATHY

Microvascular complication of DM.

Pathophysio → Hyperglycemia (1)



Stage	Duration of DM	Alb.	eGFR.	Rx
① Hyper functioning	1-5 yrs	⊖	Supra-Ⓝ > 120 mL/min.	Strict DM control ²⁸³ ①
② Silent stage	5-8 yrs	⊖	↓ Returns to Ⓝ	Adequate Hydration. + ②
③ Incipient (subclinical)	8-12 yrs	Micro albuminuria +ve	CKI stage I/II	ACEI / ARB ③

Early-EM → Thickening of GBM
non-specific to ASIS

④ OVERT (symptomatic)	12-18 yrs	GROSS	CKI Stage 3/4	Consider RRT
⑤ ESRD	18-25 yrs	GROSS	Stage ⑤	RRT is mandatory

LATE/Advanced/EM → Nodular glomerulosclerosis
irreversible (K-W - Kimmelstein - Wilson nodules)

ALPORT'S SYNDROME

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M/c - XL - (R) defect
20-40 yrs.
 $\sigma > \phi$

α_5 subunit - Type IV collagen = ABSENT

<u>H/c</u> GBM	Cochlear B.M.	Lens		Skin
G.N. ↓ Recurrent Hematuria	SNHL	H/c $\approx 75\%$ Dot & fleck retinopathy (Not specific)	Most specific Ant. Lenticonus ($\approx 25\%$ cases)	Asymptomatic

Ass - Renal Biopsy \Rightarrow "BASKET-WEAVE" appearance
of GBM.

only Rx - Renal Transplant:
 \rightarrow Never recurs in graft
excellent survival

Post-Transplant Complication - Mimic Recurrence (Hematuria)

\downarrow
(RARE) \rightarrow already on Immunosuppression] Anti-GBM disease
(Ab against α_5 subunit).

POLYCYSTIC KIDNEY DISEASE

Group of inherited Disorders characterized by ²⁸⁵

A) multiple cysts in multiple organs

Kidney

Liver

Pancreas

Spleen

B) Berry Aneurysm

↑ risk of SAH

C) Colonic Diverticuloses

↓

Recurrent Colitis.

↓

↑ oxalate reabsorpⁿ from gut

↓

Hyperoxaluria

↓

Oxalate Renal calculi

Mode of Inheritance

AD-PKD ^{M/C}

↓

Survive till adulthood
Called - adult - Polycystic KD

AR-PKD ^{Rare}

↓

Never survive >10yrs
of age

APKD-1

POLYCYSTIN - 1

Chr. 16

moderate form

20-30yrs.

APKD-2

POLYCYSTIN - 2

Chr. 4

mildest form

30-50yrs of age

PKHD (Hepatic)

Fibrocystin

Chr 6

most severe

I.V. Life / Infancy

C/F

AD

Recurrent Loins Pain M/C

+ Hematuria / fever (Infection in Renal cyst)

M/C - Extra-renal (Hepatic cysts)

- mechanical compression - Bil. radicles

- cholestasis / cholangitis

Asis USG < 30 yrs

30-59 yrs

⊕ ≥ 2 Renal cysts

≥ 4 Renal cyst

each kidney ≥ 1

≥ 2 in each

R_x - Renal Transplant

No recurrence

Good Prognosis

AR

- oligohydramnios (30% ²⁸⁶ fetal loss)

- Uremic symptoms in infancy

- ESKD ≈ 10 yrs of age

- Cirrhosis ≤ 10 yrs of age

(CAROLI'S Disease = Defect of Intra-Hepatic Biliary Radicle)

Present ≈ 30% cases

No cure

Grave Prognosis

RENAL REPLACEMENT THERAPY

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BEST FORM → TRANSPLANT

- Potential cure
- Better survival
- Better quality of Life

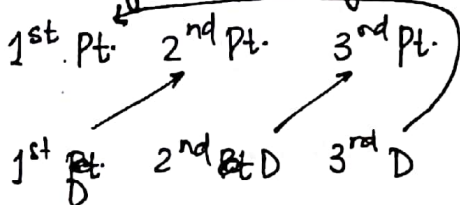
DIALYSIS

only filtration.
Palliative Rx only

↓
Limited Donor Availability

DOMINO Tx

Kidney swapping



HLA Registry

All Sx must be done on
Same calendar
(Limits - chain size)

HAPLO-Identical

(MHC/HLA matching) — 6 Ag matching

Class I	A	B	C
Class II	DP	DQ	DR

> 3 = good match.

≤ 3 = Poor match.

(Less than half match)

• Most imp. HLA match is HLA-DR
↓
Best success

DIALYSIS

HEMODIALYSIS (H.D.)

- vascular access
(Cannula, AV fistula)
- High Complications Rates
(Bleeding, sepsis, Thrombosis)

• H.D. centres

(Limited availability)

- Biocompatible - methyl cellulose polymer (filter)
(High cost)

PERITONEAL (P.D.)

- Intraperitoneal catheter placement → done ↓ LA
- Low complication rates
(≤ 1% risk → Peritonitis)

• no problem

only CI - Part H/O recurrent
CI Sx

Lower cost - omentum acts as
filter

<ul style="list-style-type: none"> • <u>Risk</u> → Infection transmission (HIV, Hep B, Hep C, CMV) 	<ul style="list-style-type: none"> • No Risk → Installing sterile peritoneal Dialysate fluid
<ul style="list-style-type: none"> • Huge Hemodynamic/osmotic shift → poorly tolerated • (M/C) acute compⁿ → <u>HYPOTENSION</u> <ul style="list-style-type: none"> - Muscle cramps / Fatigue • Sudden cardiac death <ul style="list-style-type: none"> In cardiomyopathy EF < 15% ↳ C/I 	<ul style="list-style-type: none"> • LOW SHIFTS → Better Tolerated • Safe in cardiomyopathy <ul style="list-style-type: none"> * Post cardiac Sx
<ul style="list-style-type: none"> • Risk → HYPOGLYCEMIA <p>Preferred Form.</p> <p>Excellent filtration Rate</p> <p>800-1200 mL/min</p>	<p>Risk → HYPERGLYCEMIA/ wt. gain</p> <p>Poor Filtration</p> <p>15-25 mL/min.</p> <p>only Back-up</p>

DIALYSIS ASSOCIATED AMYLOIDOSIS

- Accumulation of β_2 microglobulin (β_2 -MG)
- In the musculoskeletal system
- M/C → entrapment neuropathy
- On dialysis \approx 3-7 yrs
- Neither form (HD/PD) can filter β_2 -MG.
- X-Ray Hand - Deposits in metacarpals.
- only Rx = Renal Transplant

PRE-TRANSPLANT - Indications

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1) APIKD

2) Horse-shoe Kid

3) Obstructive uropathy

} ↑ Risk of infections in the
native kidneys

↓
Post Transplant
Immunosuppression

Septicaemia → stop Immunosuppressants

↓
Rejection of Graft

CNS

achin_mehra@yahoo.com

~~PP~~ Priyachin ~~met~~ mehra

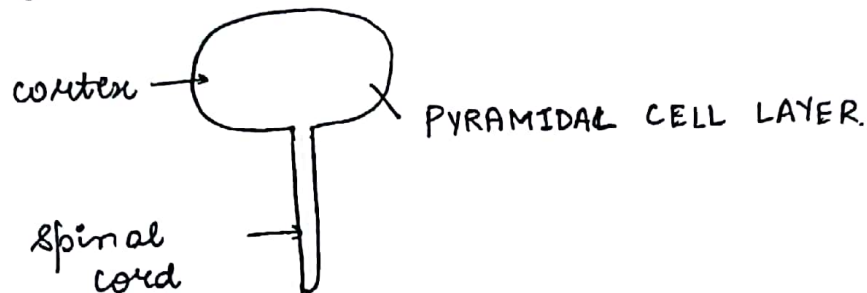
SEIZURE DISORDER & EPILEPSY ²⁹³

↓
SACURE

= to take possession of

SEIZURE

Paroxysmal event due to hypersynchronous CNS discharges



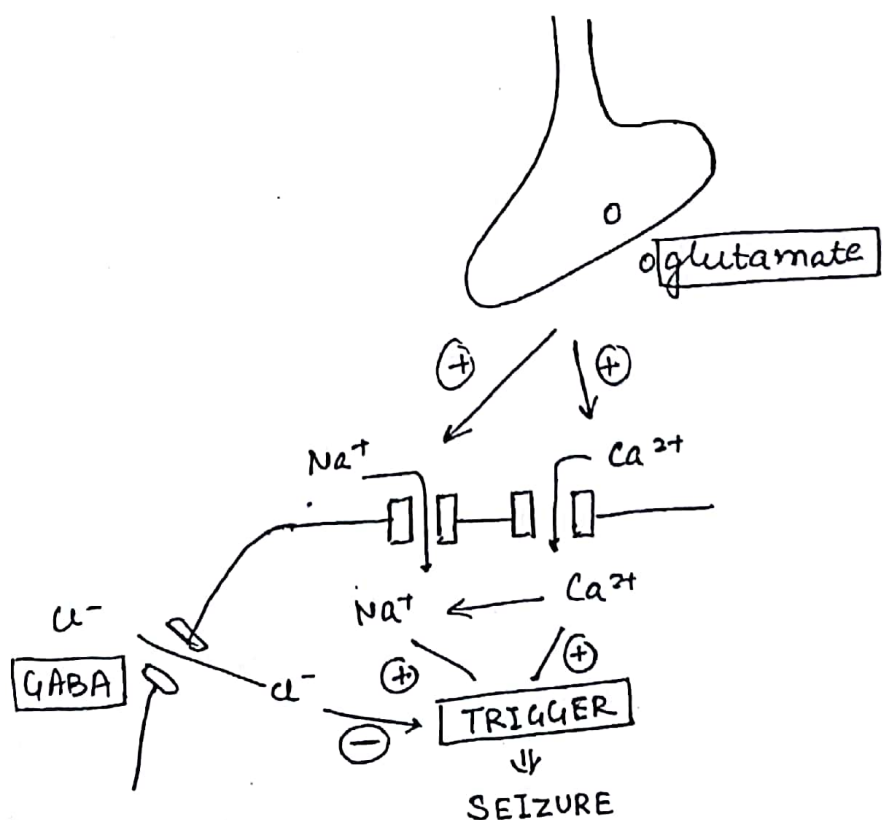
EPILEPSY

≥ 2 unprovoked seizure

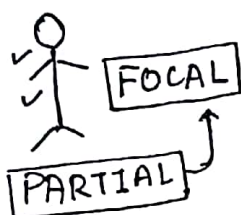
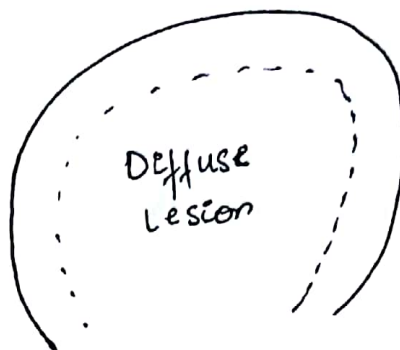
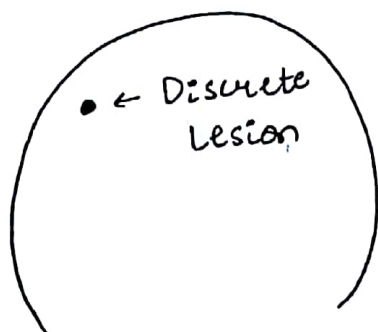
EPILEPTOGENESIS

↑ GLUTAMATE
excitatory

↓ GABA
Inhibitory



CLASSIFICATION OF SEIZURES



Structural Ab^(N)



DRUGS

Antibiotics - Quinolone

Antivirals - Acyclovir

Antimalarials → mefloquine
 ↓
 chloroquine

Analgesics - Tramadol

TOXINS

ABUSE
Cocaine

Amphetamine

→ WITHDRAWAL
Alcohol

METABOLIC

↓ Na⁺ (H/c Biochemical Ab[⊕] ppt. seizure)

(↓ seizure)
due to cerebral edema
↑
↓ 100

<100

2) $\uparrow K^+$, $\downarrow K^+$ \Rightarrow doesn't cause seizure.

FOCAL SEIZURES

LOSS OF CONSCIOUSNESS

||
Contact

||
Cognition

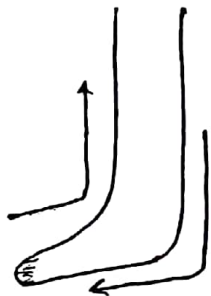
→ (+) = Dys cognitive (complex) ← PARTIAL
→ (-) = Non Dys cognitive (simple) ←

TODD'S PALSY

- Post Ictal Paralysis
- Self recoverable

↳ starts in 1st 24 hours of onset

FOCAL SEIZURE



Distal → Proximal

JACKSONIAN MARCH

→ focal seizure arising from in a Limb.

GENERALISED

ABSCENCE SEIZURE / PETIT MAL EPILEPSY

MYKNOLEPSY

- Loss of contact & environment
- Tone of Body (N)
- Abrupt onset
- ≤ 30 Sec
- Subtle Motor Signs (+) (minor)
- AURA (-)
- NO post ictal confusion

Starts - 4-8 yrs of age

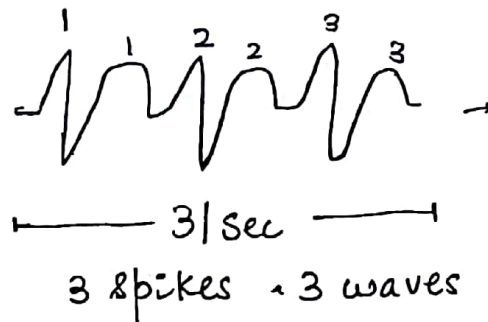
296

Spontaneous Remission

in 60-70% by 18 years of Age

EEG :- B/L 2-4 Hz spike & wave

Precipitated by Hyperventilation.
(1-3 min)



↓
SPIKE & DOME pattern
or
spike & wave "

ATYPICAL ABSCENCE SEIZURE

- Loss of consciousness - Less abrupt
↑ Duration.
- mental Retardation
- Structural Ab(Ⓢ)
- EEG - ≤ 2.5 Hz spike & wave
(slow)
- Resistant to Anti epileptic Drug

MYOCLONIC SEIZURE

↓
Jerky movement

- CAUSE -
- 1> Hypoxia
 - 2> Degenerative

H/o Hanging → Compresses Carotid

297

↓
Cause hypoxia.

000 JUVENILE MYOCLONIC EPILEPSY

- Early Adolescence
- Family H/o
- Chromosome No. 6
- unknown cause. ⇒ x hypoxia
x Degeneration.

- B/L Myoclonic jerks
 - └ on awakening
 - └ ppt by
 - └ Fatigue
 - └ Alcohol

- IQ (N)

→ Loss of consciousness (N)

→ subtle motor signs (N)

- └ eye Blinking
- └ Lip smacking

[AUTOMATISM]

MAJORITY may turn into GTCS. pt

GENERALISED TONIC CLONIC SEIZURE

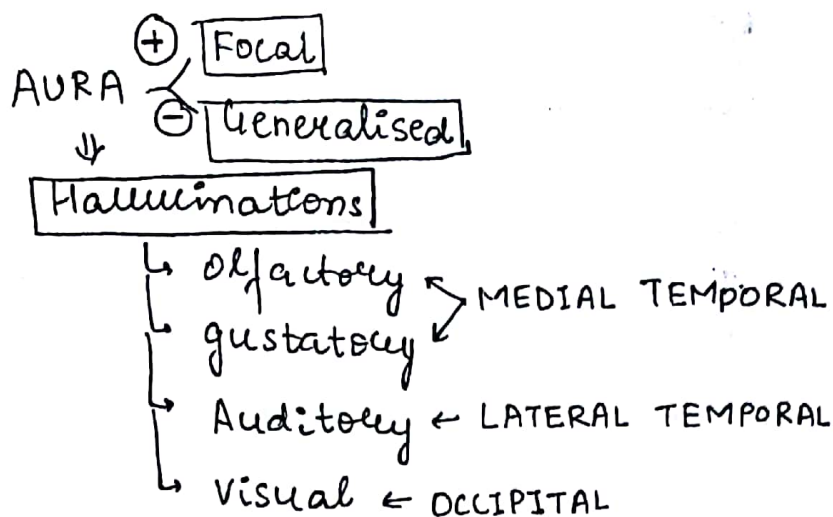
GRAND MALL EPILEPSY

PREMONITARY SYMPTOMS-

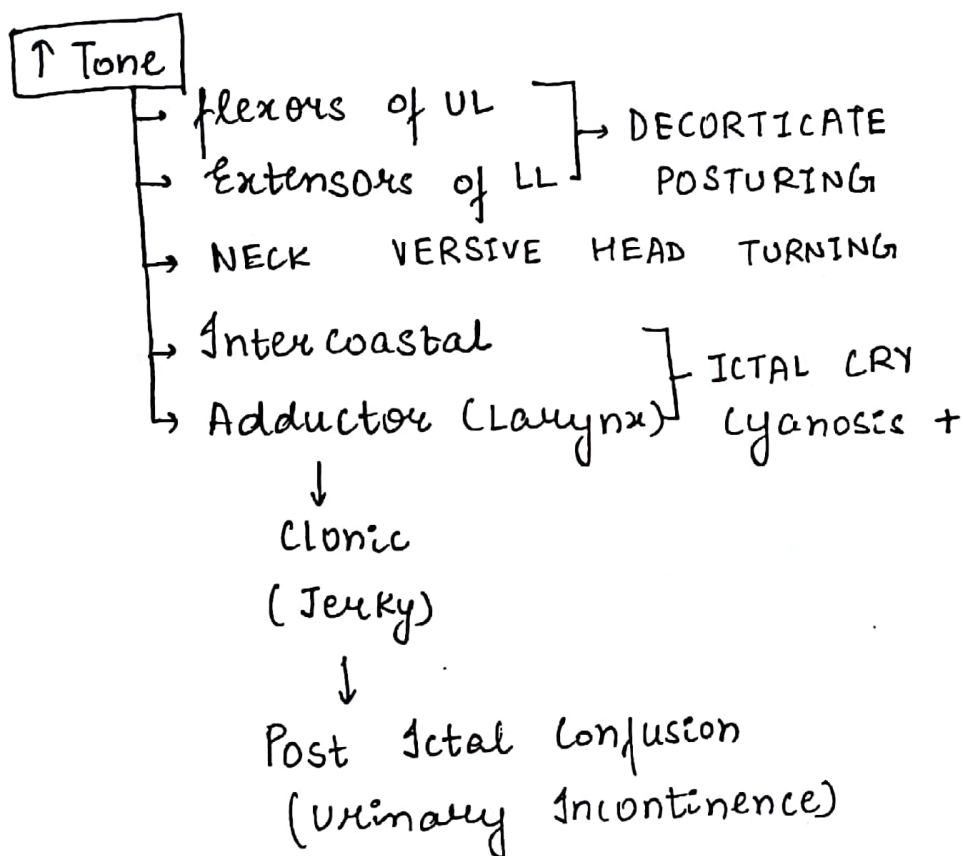
Nausea

vomiting

Abdominal Pain



[NOTE: Aura seen in Focal Lesions.]



JUVENILE MYOCLONIC EPILEPSY

- Myoclonus
- Majority → GTCS
- $\frac{1}{3}$ rd → Absence seizure

M/c presentation of JME is MYOCLONUS (AZIMS₂₉₉)

MESIAL TEMPORAL LOBE EPILEPSY

→ Focal seizure \bar{c} Loss of consciousness [DYS COGNITIVE]

→ DEJA VU

→ Febrile seizure.

→ Enlarged Temporal Horn
Small Temporal Lobe
Hippocampal sclerosis

R_x $\left\{ \begin{array}{l} R_{xOC} = S_x \\ \text{antero-medial} \\ \text{part removed} \end{array} \right.$
Temporal Lobectomy
Amygdalo
Hippocampectomy

→ Resistant to anti-epileptics

S. PROLACTIN

↑ 30 mins after True seizure

ANTI-EPILEPTIC DRUG

A.E.D. X 2 years $\xrightarrow{\text{TAPER}}$ 3rd year
↓
Stop.

Sudden withdrawal of drug \Rightarrow ppt. seizure.

Seizure ppt. while withdrawal in 1st 3 months. more commonly.

X DRUG

Provoked

1st episode of seizure

✓ DRUG

Unprovoked

→ Febrile seizure

→ Alcohol withdrawal

↓
BZD → Injectable

→ Status epilepticus

→ Family H/o (+)

→ Abn neurological exam

Chlordiazepoxide

Oral

for gen. alcohol. withdrawal

not for seizures

Ab(N)-EEG

CT/MRI.

300

IOC

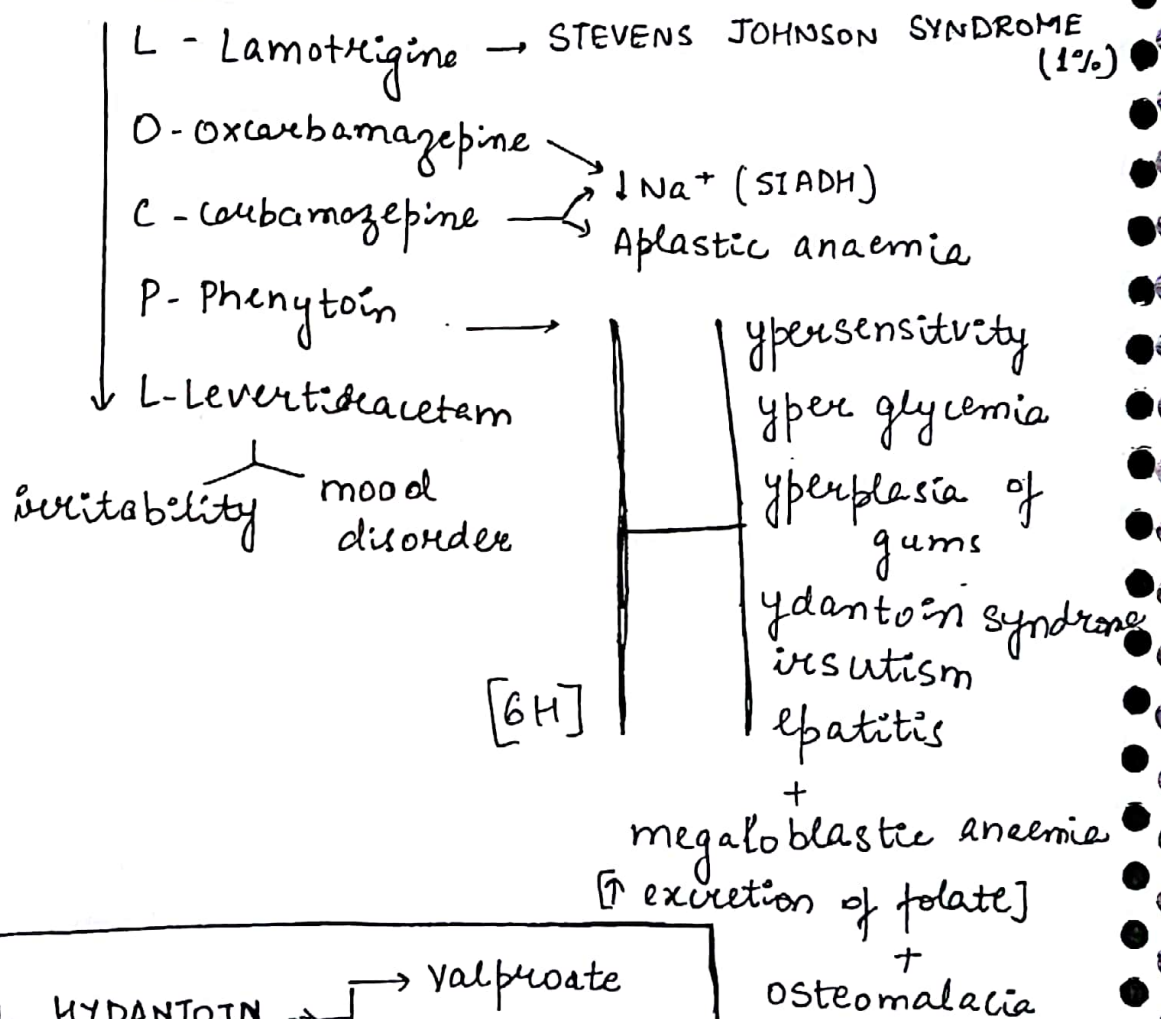
Seizure \Rightarrow EEG

DOC =

\uparrow EFFECT

\downarrow SIDE EFFECT

FOCAL



FETAL HYDANTOIN \rightarrow

Microcephaly

Hypoxia of Limbs

Cleft \leftarrow Lip
Palate

\rightarrow Valproate
 \rightarrow Phenytoin
 \rightarrow carbamazepine

GTCS

Valproate
 Lamotrigine
 Topiramate

ABSCENCE

ETHOSUXIMIDE - DOC

Valproate
 Lamotrigine

ATYPICAL ABSENCE SEIZURE

ooo

**SAFEST A.E.D**

Lamotrigine > Carbamazepine > Pheno barbitone
 ↓ teratogenic
 ↑ sedative even for fetus

DOC → as per seizure type
 monotherapy

Lowest effective Dose

GTCS → Valproate → Neural Tube Defect → (N) Preg = 1-2%
 ↓
 A.E.D. = 10-20%

A.E.D is not 100% Teratogenic

Do not change Rx During ♀ becoz changing Rx can ppt seizure [Break through].

Seizure frequency during ♀

50% - Unchanged

20% → ↓

30% → ↑

↓ emesis,

$\gamma \uparrow$ in 30%

302

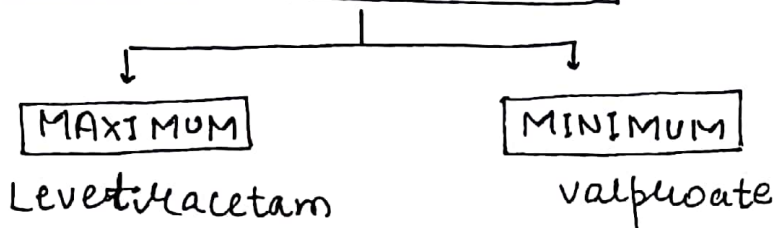
1) Emesis \rightarrow ↓ absorption of drug

2) Hormones

Progesterone
 \uparrow seizure
threshold

Estrogen [epileptogenic]
 \downarrow seizure
threshold

A.E.D. Excreted In Breast Milk



Breast feeding is recommended

AED is also continued

JME

A.E.D. x Lifelong

DOC = Valproate

Levetiracetam

\Rightarrow DRUGS NOT USED IN JME

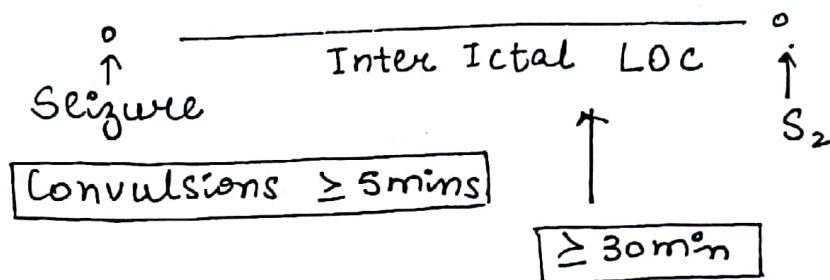
\rightarrow Carbamazepine
 \rightarrow Phenytoin
 \rightarrow Lamotrigine

} $\rightarrow \uparrow$ myoclonus

\Rightarrow PRE \odot on valproate
 \downarrow change to
Levetiracetam

STATUS EPILEPTICUS

303



EPILEPSIA PARTIALIS CONTINUA

⇒ Continuous partial seizure

⇒ Status epilepticus in focal seizure

1st Drug LORAZEPAM or MIDAZOLAM
 (0.1 mg/kg) ^{Doc} (0.2 mg/kg)

↓
 I.V. A.E.D. x Dextrose ⇒ Phenytoin ppt's
Normal Saline = dextrose

PHENYTOIN
 20 mg/kg @ 50 mg/min
 ↓
 0 order kinetics cardiotoxic

→ POs PHENYTOIN
 @ 150 mg/min
 ↓ Hypersensitive
 mixed = Dextrose
 I/M

OR
VALPROATE
 (25 mg/kg)

OR
LEVETIRACETAM
 (20-30 mg/kg)

[POST - TRAUMATIC EPILEPSY] → LEVETIRACETAM.
 ↓ + Seizure

I.V. MIDAZOLAM
 0.2 mg/kg → 0.2-0.6 mg/kg/hr

OR
I.V. PROPOFOL
 ↓ + Seizure

↓
THIOPENTONE

CARBAZEPINE → not recommended in status
as found in oral form

MOVEMENT DISORDERS

ATHETOSIS / CRAWLING

- slow
- sinuous
- writhing
- seen in Lesions of GLOBUS PALLIDUS ⇒ G A P

CHOREA / DANCE like movement

Semi purposeful movement

Lesion - CAUDATE NUCLEUS

↑
CORPUS STRIATUM

CAUSES -

C - Chorea gravidarum

H - Huntington's Chorea

O - OCP

R - Rheumatic / Sydenham's Chorea

E - Endocrine / Thyrotoxicosis

A - Atherosclerotic / Senile

M/c/c ⇒ SLE

HEMIBALLISMUS \Rightarrow Exclusively on ONE SIDE

305

- ✓ Large Amplitude
- ✓ Flinging
- ✓ Proximal
- ✓ Limb

✓ Lesion \Rightarrow SUBTHALAMIC NUCLEUS (STN)

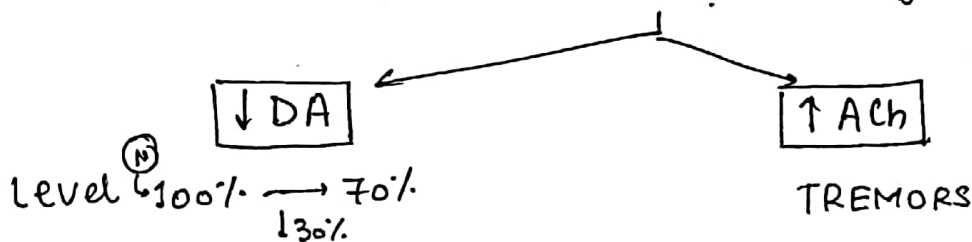
\Downarrow
C/L

PARKINSONISM

Degeneration / Atrophy \Rightarrow SUBSTANTIA NIGRA
PARS COMPACTA (SNPC)

\Uparrow
LEWY BODY

- \rightarrow Intra-neuronal
- \rightarrow Intra-cytoplasmic
- \rightarrow Eosinophilic inclusion Body
- \rightarrow Contains α synuclein



RIGIDITY

ETIOLOGY:-

1) DRUGS \Rightarrow DA \ominus
(H/c of
2° Parkinsonism)

TYPICAL ANTIPSYCHOTICS

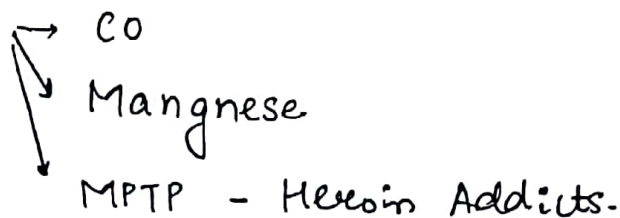
Haloperidol

CPZ

METOCLOPRAMIDE

DA Depletors \Rightarrow Methyl dopa
Reserpine

27 TOXINS

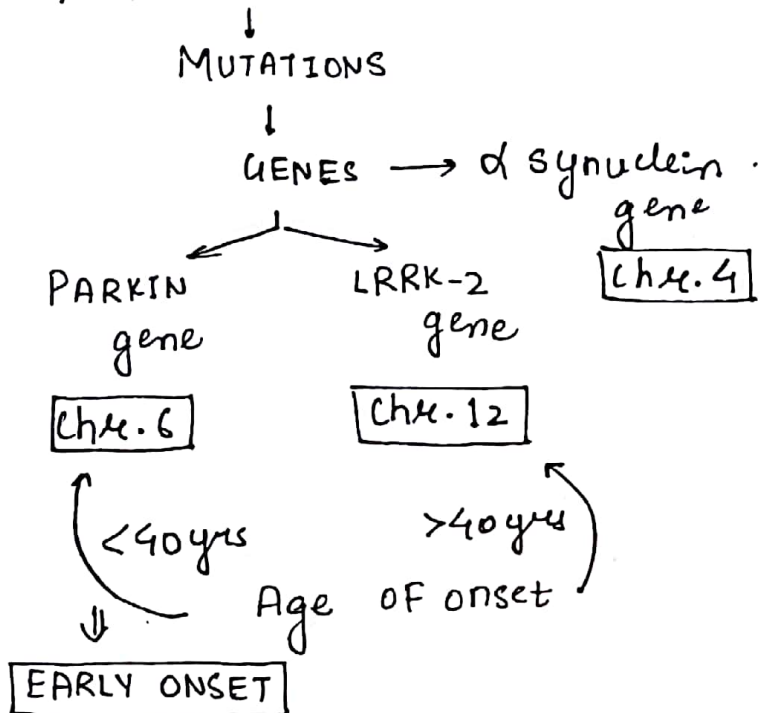


306

37 TRAUMA

BOXERS

47 FAMILIAL / GENETIC

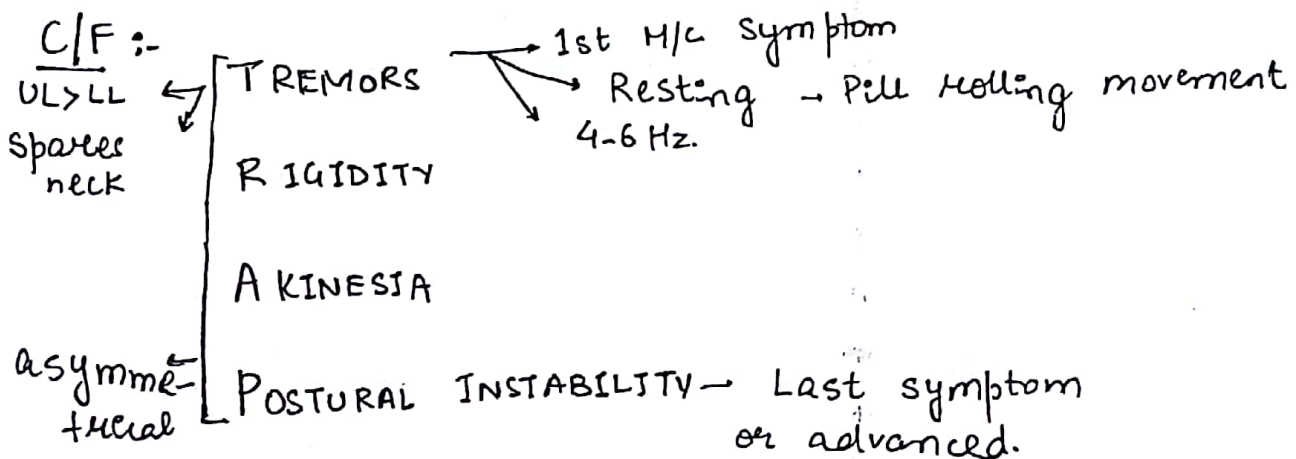


57 IDIOPATHIC -

85-90% pts.

↓
PARKINSON DISEASE. (M/c type)

"
PARALYSIS AGITANS



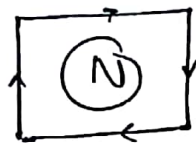
TITUBATION \rightarrow \ominus Parkinsonism
 $\downarrow \oplus$
 cerebellum

307

TREMOR

RESTING TREMOR \Rightarrow PARKINSONISM

INTENTIONAL TREMOR \Rightarrow CEREBELLAR LESIONS



FLAPPING TREMOR = HEPATIC ENCEPHALOPATHY
 "ASTERIXIS" UREMIA "
 CO_2 narcosis

FINE TREMORS = THYROTOXICOSIS

BENIGN ESSENTIAL TREMORS

- \rightarrow 5 - 11 Hz
- \rightarrow AD inheritance
- \rightarrow VL > LL
- \rightarrow ORIGIN = cerebellum
- \rightarrow \uparrow anxiety
- \downarrow on alcohol consumption
- = Rx \rightarrow Propranolol



RIGIDITY - BEST Jt to show Rigidity = WRIST

Resistance to passive movement

LEAD PIPE \rightarrow EXTRA PYRAMIDAL SYNDROME

superimposed

tremors

on
rigid lead
pipe

COG WHEEL \rightarrow PARKINSONISM

\rightarrow UL = COG WHEEL

\rightarrow LL = LEAD PIPE

CLASP KNIFE - UMNL

RIGIDITY

Tone ↑ Flexors = Extensors
Bidirectional

SPASTICITY

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Flexors > Extensors
Unidirectional
velocity Dependent

GAIT

FESTINATING GAIT → Parkinsonism

(ready to run)

Kinesia Paradox

↳ ↑ acceleration on running

+ spasticity
↑
wk. Distal > Proximal

CIRCUMDUCTION GAIT - Hemiparesis → corticospinal tract

WADDLING GAIT - Myopathy (Proximal)

Lurching GAIT - Polio Lesion → Ant. Horn cells.

BROAD BASED - Cerebellum → Drunken Gait

HIGH STEPPAGE - Foot Drop] neuropathy
Deep Peroneal N/V

STAMPING → TABES DORCALIS

↳ lesion → post column

loss of vibration

POSTURAL INSTABILITY

Loss of Postural Reflexes → FALL

MICROGRAPHIA

Small handwriting

(N) I am a doctor

(PD) I am a dent-

MONOTONOUS SPEECH

309

Hypophonia

MASK LIKE FACE

Depression

Dementia

SYMMETRICAL
↳ unresponsive to
Levodopa

PARKINSONISM + ATYPICAL PK

1> Progressive Supranuclear Palsy / STEEL RICHARDSON SYNDROME

- Extended Posture
- Defective Downward Gaze
- H/o fall ← early in this type
- Dementia
- ⊖ Tremors

2> LEWY BODY DEMENTIA (LBD)

Parkinsonism + Visual Hallucination

3> MULTIPLE SYSTEM ATROPHY (MSA)

Parkinsonism + cerebellum + Autonomic
Symptom Instability

4> CORTICOBASILAR DEGENERATION (CBD)

Parkinsonism + myoclonus + Dystonia
sustained Posturing

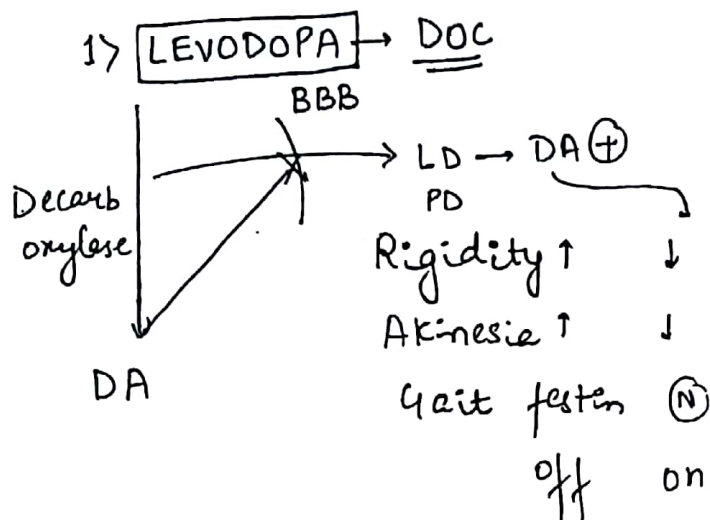
Rx

310

↓ DA
(rigidity)

PD

↑ ACh
(Tremor)



8) ANTICHOLINERGICS
TRIHENXYPHENYDYL

2) PERIPHERAL DECARBOXYLASE
INHIBITORS

→ CARBIDOPA
→ BENSERAZIDE

3) MAO B ⊖

→ SELEGILINE
→ RESAGILINE
(neuroprotectors)

3) COMT ⊖

→ ENTACAPONE
→ TOLCAPONE

5) AMANTADINE

↑ DA Level

6) DA + D₂

→ PRAMIPIRAZOLE
→ Ropinirole
→ Rotigotin

7) APO MORPHINE

311

↓ sedative DA ⊕
 Injectable off
 ↓
 on RESCUE
 THERAPY

CEREBROVASCULAR ACCIDENT (CVA) STROKE

→ Focal neurological Deficit due to vascular cause > 24 hrs

→ TIA (Transient Ischaemic Attack) -

< 24 hrs

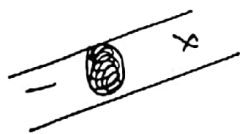
most → for 1 hour

20 mL/100gm brain tissue/min = Ischaemia +
Infarction ⊖

16 mL/min × 1 hour = Infarction ⊕

0 mL/min × 4-10 min = DEATH

CLASSIFICATION



ISCHEMIC (85%)

EMBOLIC
(75%)

THROMBOTIC
(25%)

M/c/c

AF

non-rheumatic

AF

Most epileptogenic stroke

embolic > H²ge > thrombotic

↓
cerebral edema



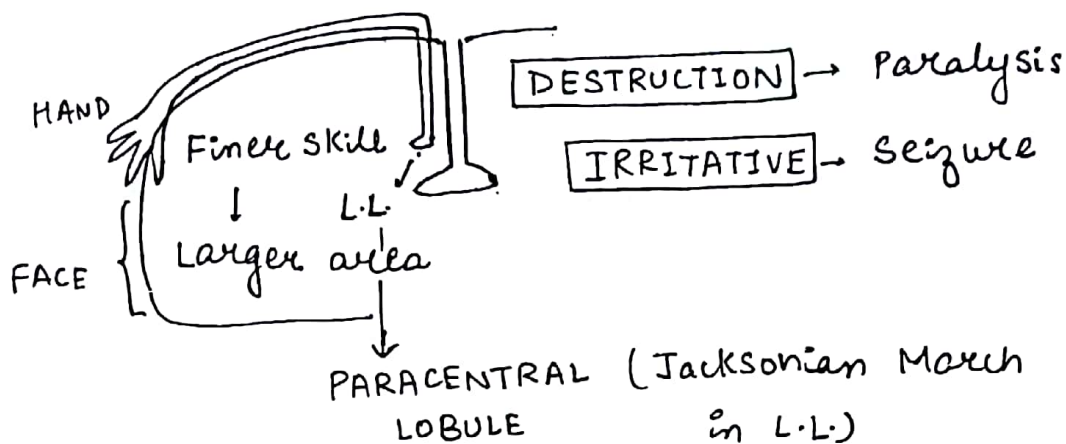
HAEMORRHAGIC (15%)

Lacunar Infarcts: subcortical
So no seizures

312

FRONTAL LOBE

1) 1^o MOTOR AREA



2) MICTURITION AREA

? where

⊖ Social Inhibition

LESION

↓ Incontinence

[Infant Bladder]

3) SUPPLEMENTARY MOTOR AREA

⊖ Primitive Reflexes

⊕ Sucking
⊕ Grasping

LESION

↓ [Resurgence of Primitive Reflexes]

4) BROCA'S AREA

→ word area

→ Located in Inf. Temporal Gyrus

5> PRE FRONTAL AREA

LESION

313

CONTROL

[ANTI SOCIAL BEHAVIOUR]

EMOTIONS

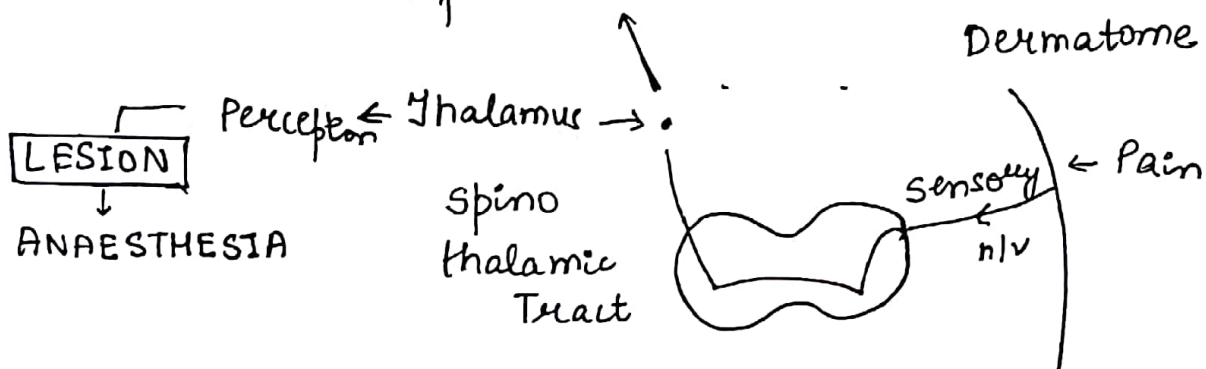
FORMED → Limbic system

CIVIC LOBE = FRONTAL LOBE

PARIETAL LOBE

1> 1° SENSORY AREA

Localisation of stimulus



2>

STEREOGNOSIS

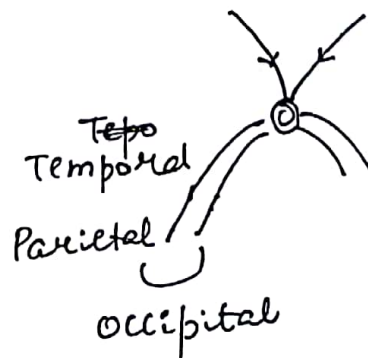
Ability to identify on touch.

3> TASTE

LESION → DYSGUSIA

4> OPTIC RADIATION

↓
SCOTOMA



5) ANGULAR GYRUS

314

Stores images a/c

→ Reading

→ Calculation

→ Naming Fingers

LESION

DEVELOPMENTAL

a) R to L Confusion

b) DYSGRAPHIA (Reading)

c) DYSLEXIA (Learning)

d) ACALCULIA

e) Finger AGNOSIA
Cannot Identify

(N) B O M B A Y

B O M B A Y

R to L confusion

GERSTMAN SYNDROME

↓
Lesion = L Hemisphere

TEMPORAL LOBE

1) 1° AUDITARY AREA

Hearing ↓

LESION → CORTICAL DEAFNESS

2) WERNICKE'S AREA

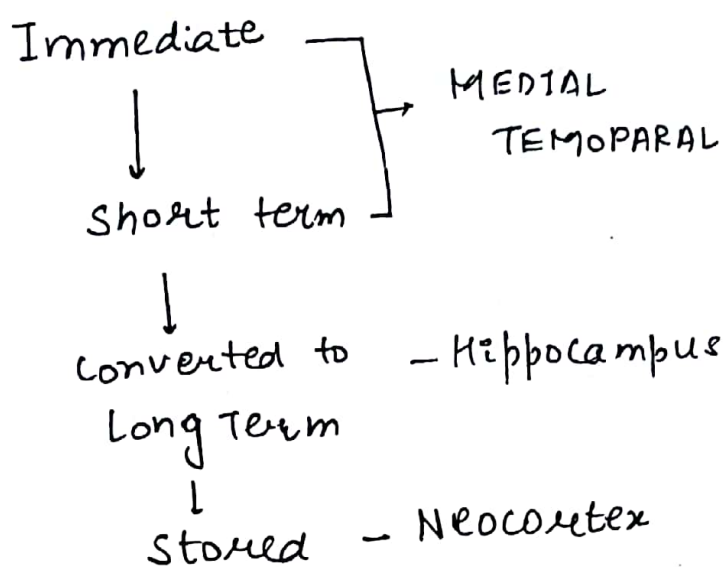
Sup. Temporal Gyrus
Comprehension

3) OLFACTION → ANOSMIA

4) OPTIC RADIATION → SCOTOMA

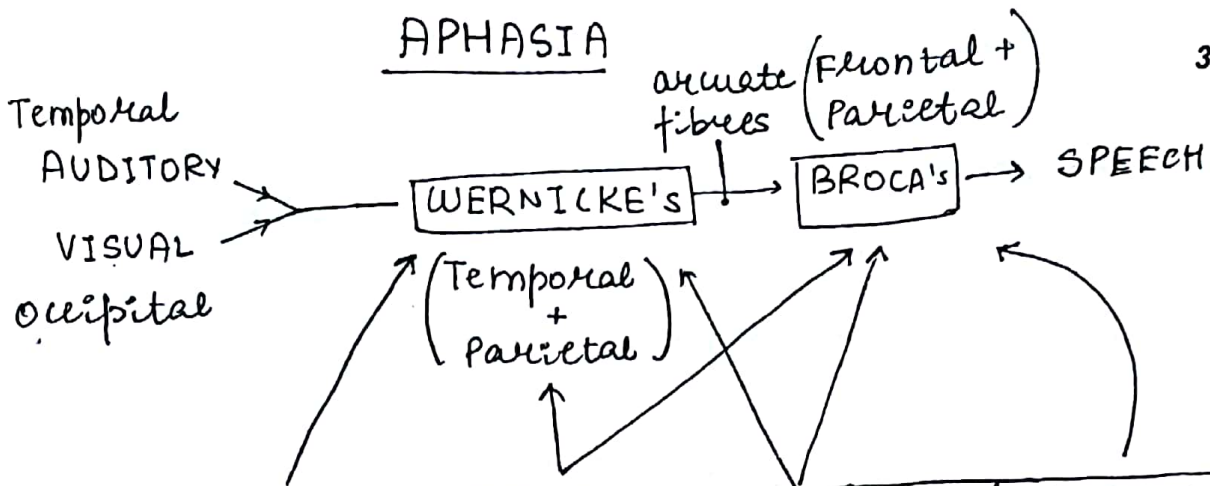
5) DEEP/MEDIAL TEMPORAL LOBE Memory

MEMORY



APHASIA

316



APHASIA	COMPR.	NAMING	REPETITION	FLUENCY
WR.	⊖	⊖ Neologism	⊖	Ⓝ/↑ EXPLOSIVE Jargon speech
BROCA	Ⓝ	⊖ Telegraphic speech Melodic Circumlocution speech	⊖	↓ Insight ⊕ Depression
CONDUCTION ↓ arcuate fibres damaged	Ⓝ	⊖	⊖	Ⓝ
TRANS CORTICAL Sensory (Post)	⊖	⊖	Ⓝ	Ⓝ/↑
Trans cortical Sensory Motor (Anterior)	Ⓝ	⊖	Ⓝ	↓

Mixed Trans cortical (Isolation aphasia)	(-)	(-)	(N) Echolalia	(-)
Pure Word Deafness Auditory Damage	(-)	(N)	(-)	(N)
Pure Word Blindness (Alexia)	↓ Reading	(N)	(N)	(N)
Anomic Aphasia	(N)	(-)	(N)	(N)

→ M/c type
angular gyrus

seen in

Alzheimer
Head Trauma
Metabolic
encephalopathy

SCANNING speech I AM A DOCTOR
↳ CEREBELLAR Lesion.

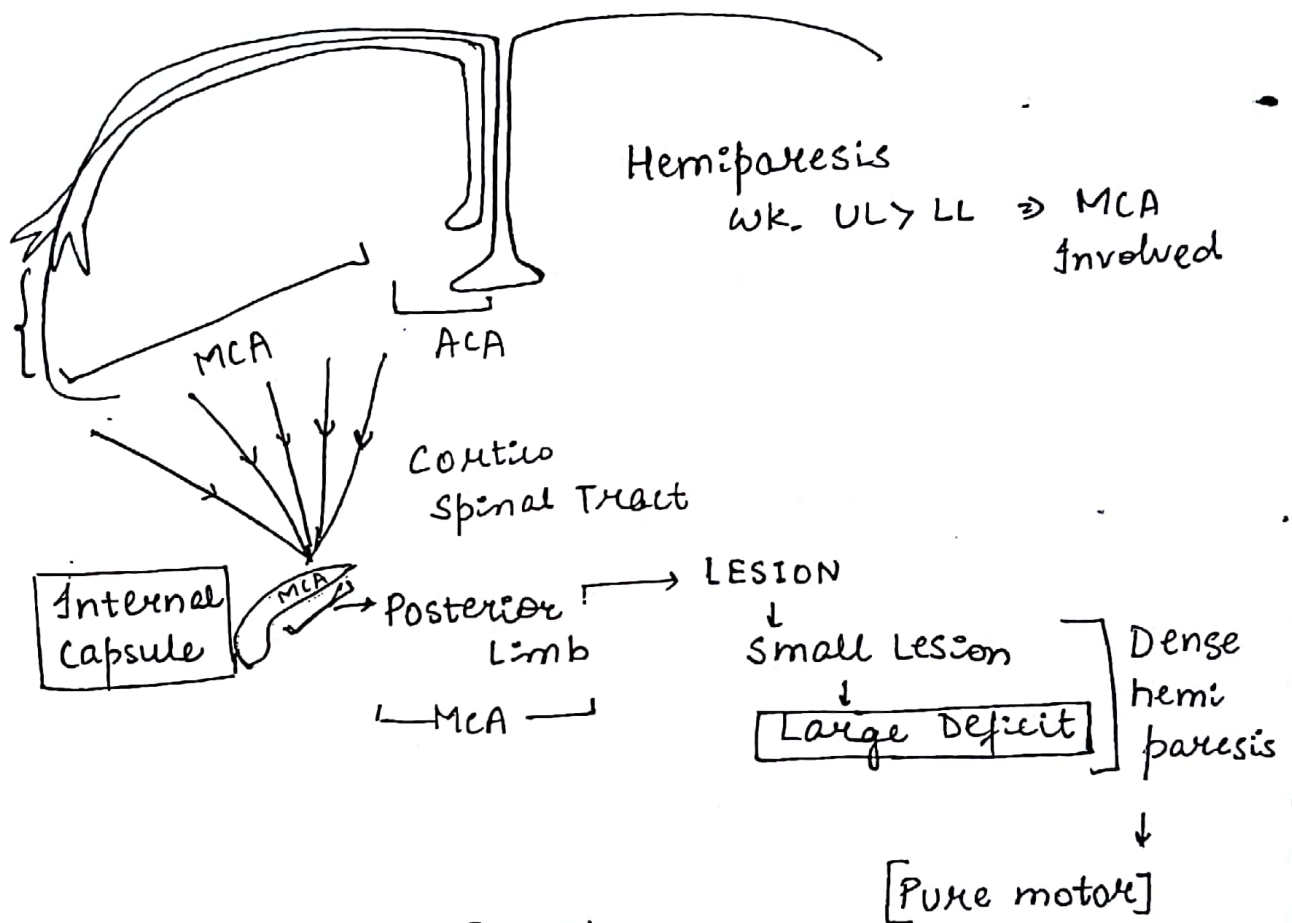
⇒ Broca's Lesion ⇒ couldn't write a Dictation

Ant Cerebral Artery

318

FRONTAL

- Paracentral lobule → L.L. weakness, Incontinence
- Supplementary motor → Primitive Reflexes (+)
- Prefrontal → Antisocial Behaviour



APHASIA → MCA (L) → Broca's, Wernicke's

AMNESIA → Post. cerebral artery → medial Temporal, Hippocampus

GAIT APRAXIA → Ant. cerebral artery
↳ ⊖ movement

R_x [ISCHEMIC]

319

1> THROMBOLYSIS

Recombinant tissue Plasminogen activator (rtPA)

(I.V.) = 0.9 mg/kg

10% → Loading Dose
90% → Infusion × 1 hour

MAX DOSE = 90 mg/kg

WINDOW PERIOD = 4.5 hours
from onset

2> ANTIPLATELETS

ASPIRIN

NO clopidogrel

3> ANTI COAGULANTS

HEPARIN

↓

WARFARIN

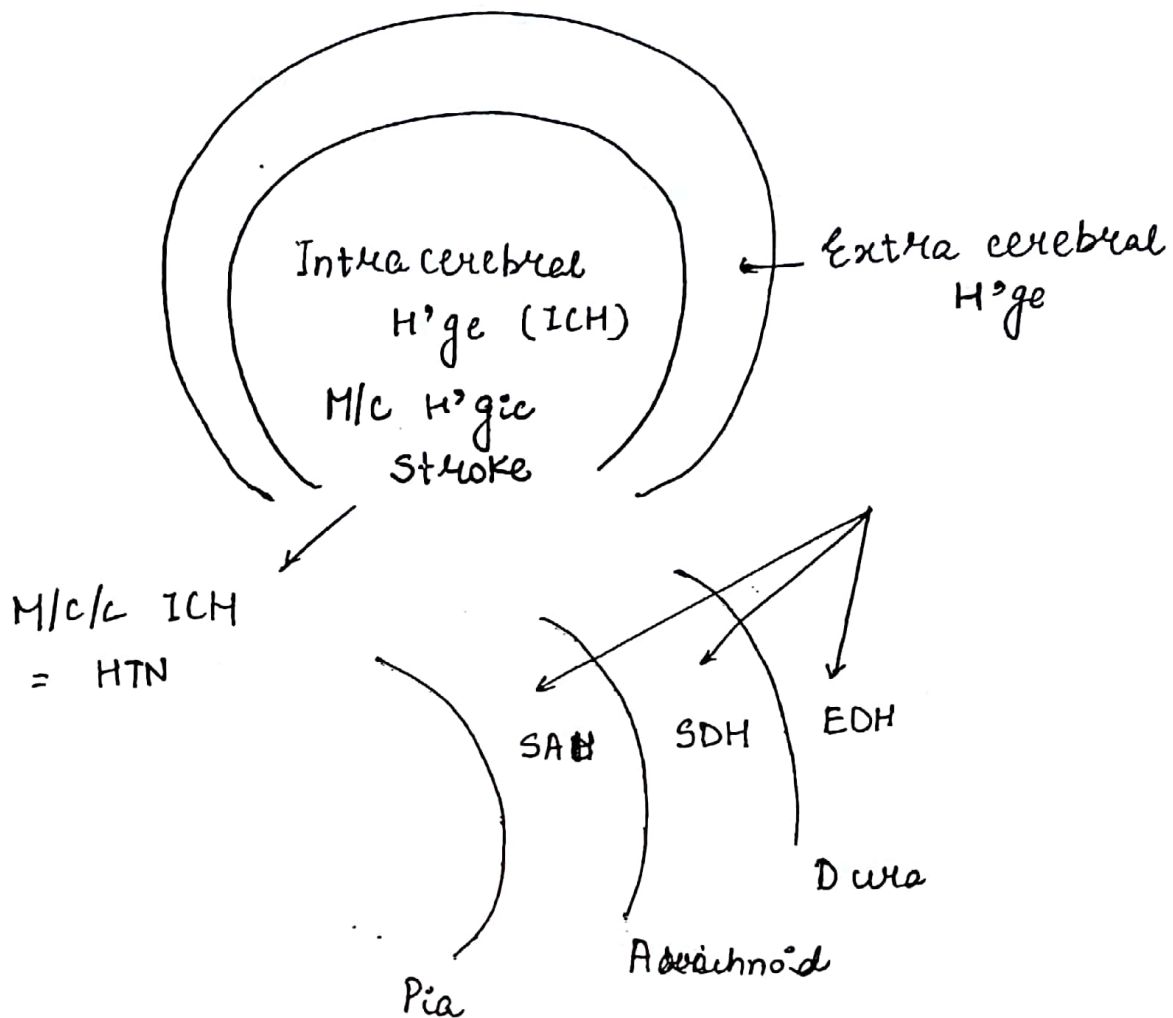
AF
Prosthetic valve

B <u>POWER</u>	
GRADING (MRE scale)	
0	→ no movement
1	→ flickering
2	→ with gravity eliminated
3	→ against gravity
4	→ against Resistance
5	→ NORMAL

Power

↑ (1/5 → 4/5) ⇒ EMBOLIC

↓ (4/5 → 1/5) ⇒ THROMBOTIC



HTN ICH

SITES

1) Basal Ganglia (Putamen)] ^{M/c site} HEMI PARESIS

2) Thalamus ← HEMI ANAESTHESIA

3) Cerebellum ← ATAXIA] ^{Rx} Decompression
 VERTIGO] diameter > 3cm

Worst

Prog 4 Pontine

B/L extensor
Plantar

↑
HR
RR
Temp
Sweating



PIN POINT → OP Poisoning

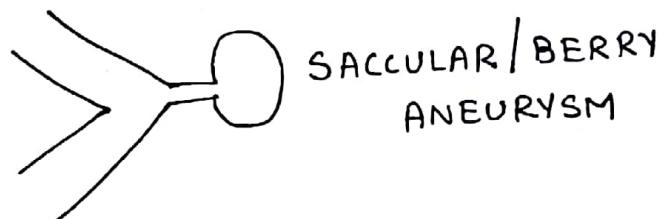
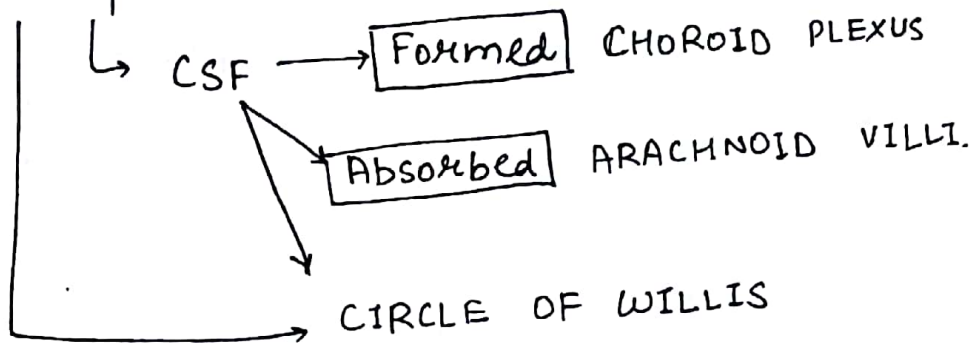
PUPIL → morphine

* also seen in -

000 SAH H²ge

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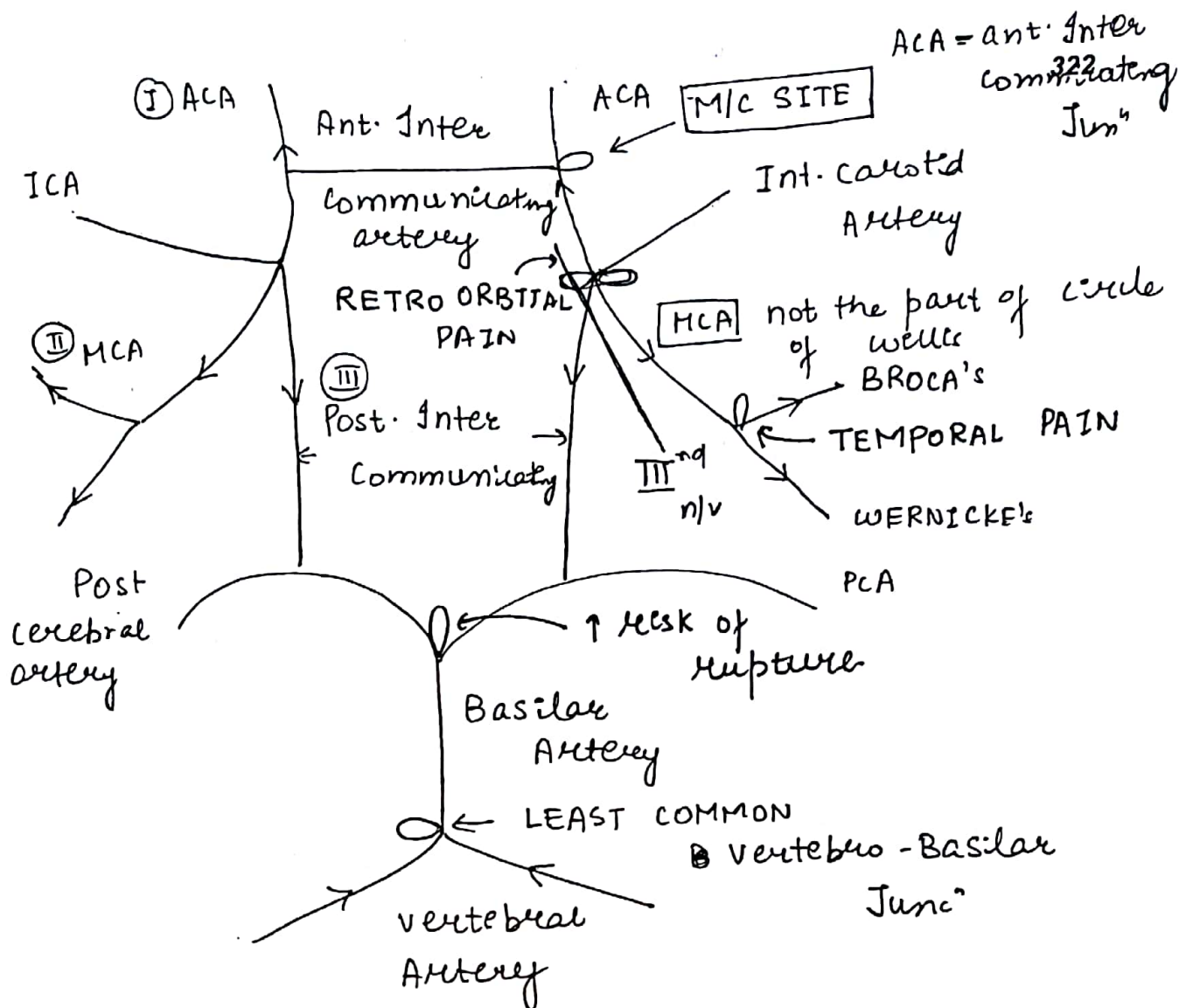
S. A. space



ETIOLOGY

- 1> Trauma (M/C/C).
- 2> Rupture of Berry Aneurysm (M/C/C spontaneous SAH) (non-traumatic)
- 3> A-v malformations
- 4> Extension from ICH
- 5> Idiopathic

- LOCATION = Perimesencephalic cistern
- Angiography ⇒ (N)
- Source = venous



85% of aneurysm ⇒ ANT. CIRCULATION

15% of " ⇒ **POST. CIRCULATION**

↓
Less Common

↑ Risk of Rupture

M/c cranial n/v

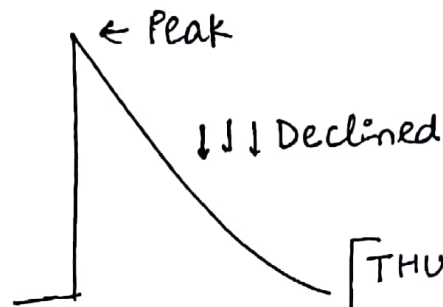
- | | |
|------------------|---------------------|
| ↳ Berry Aneurysm | ⇒ III rd |
| ↳ ↑ ICT | ⇒ VI th |
| ↳ GBS | ⇒ VII th |
| ↳ DM | ⇒ III th |
| ↳ HIV | ⇒ VII th |
| ↳ Sarcoidosis | ⇒ VII th |

Paralyzed
= VIIth

C/F-

Onset / Immediate

323



[THUNDER CLAP
HEADACHE]

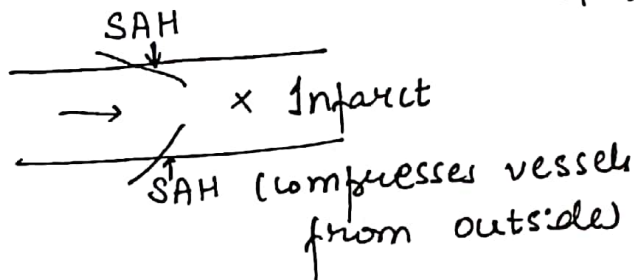
Neck Rigidity

Loss of consciousness (transient)

No focal neurological
Deficit

DELAYED

1> Vasospasm

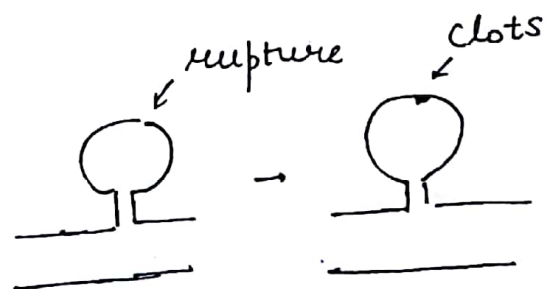
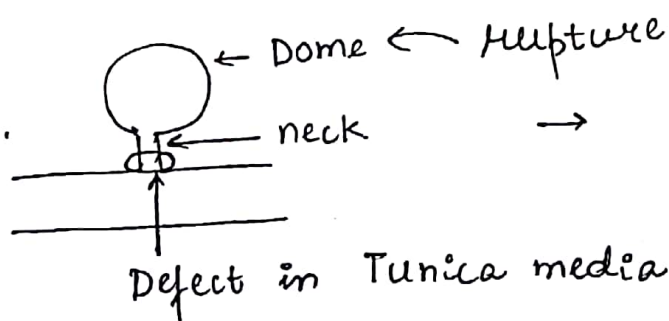


4-14 days after SAH

↓
Peaks in 1st 7 days
of onset

M.C.C. → mortality
 → morbidity

2> Re ruptured



may
rebleed
if
undetected

30% Re-rupture in 1st month

Peaks in 1st 7 days.

3> HydrocephalusSAH → BLOOD

Blocks → ↓ CSF Absorption
 Arachnoid villi
 ↓
 ↑ ICT

4> ↓ Na⁺ Hypovolemia

↑ ICT → BNP
 CEREBRAL SALT
 WASTING DISEASE

↓ Na⁺ ← H₂O ↓

INVESTIGATIONSNEUROIMAGINGCT

Acute H₂O (clot)
 Calcified

MRI

Inflammation
 Infarction
 Ischaemic

IOC → CVA → NCCT (Brain)
 [To exclude acute H₂O]
 ↓ (N)
 Infarct. → MRI (Brain)
 [To exclude acute infarct]

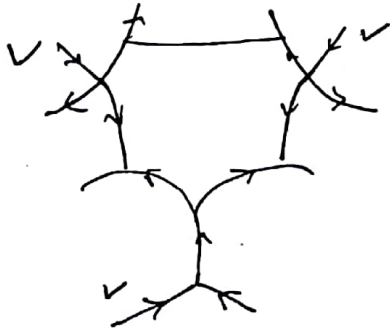
IOC

325

Acute SAH = NCCT (Brain)

Aneurysm = ANGIOGRAPHY

↳ DYE → MR angio
⊖
⊕



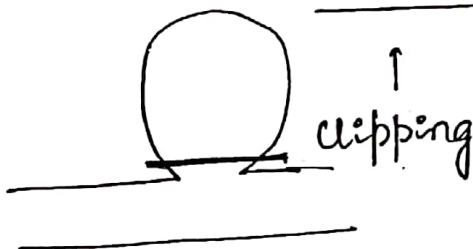
4 vessel angio
↓
2 ICA
2 VA
↓
Injected
↳ 2 ICA + 1 VA.
↓
via femoral vein

Digital Subtraction Angiography (DSA)
Subtract Bone

R_x

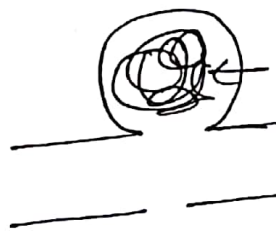
SURGICAL

TITANIUM



↑
clipping

PLATINUM



↑
coiling (BETTER)



WIDE NECK = clipping

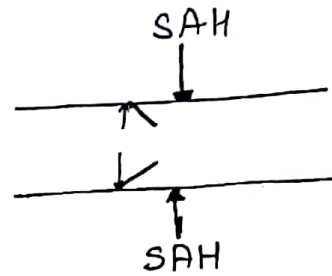


narrow neck = coiling

⇒ NIMODIPINE ⊖ vasospasm

↓
Intracerebral

⇒ (3H) → HTN [160/90]
→ Hypervolemia
→ Hemodilution (I.V. fluid)



SDH

occurs due to rupture of cortical Bridging Veins

EDH

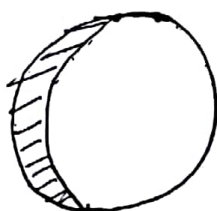
Rupture of middle meningeal artery (MMA)

HEAD INJURY (closed)

↓
Headache
+ neurological Deficit

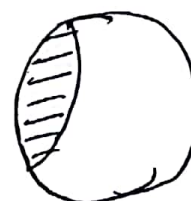
↓
Progresses

←
Days - weeks - months
slowly



SEMILUNAR

→
Hours - minutes
Rapidly



LENTICULAR

SDH

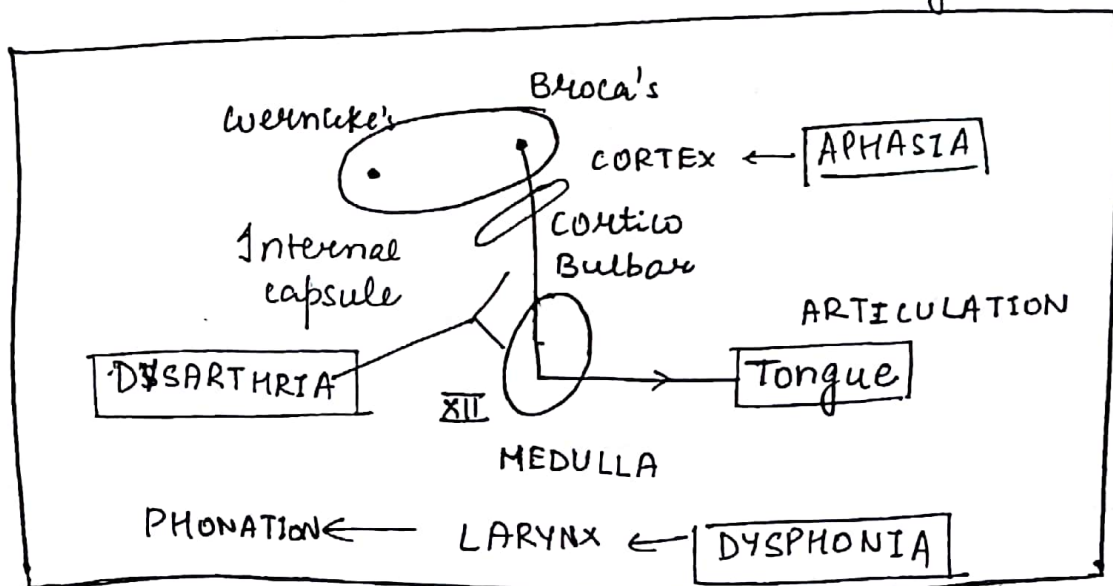
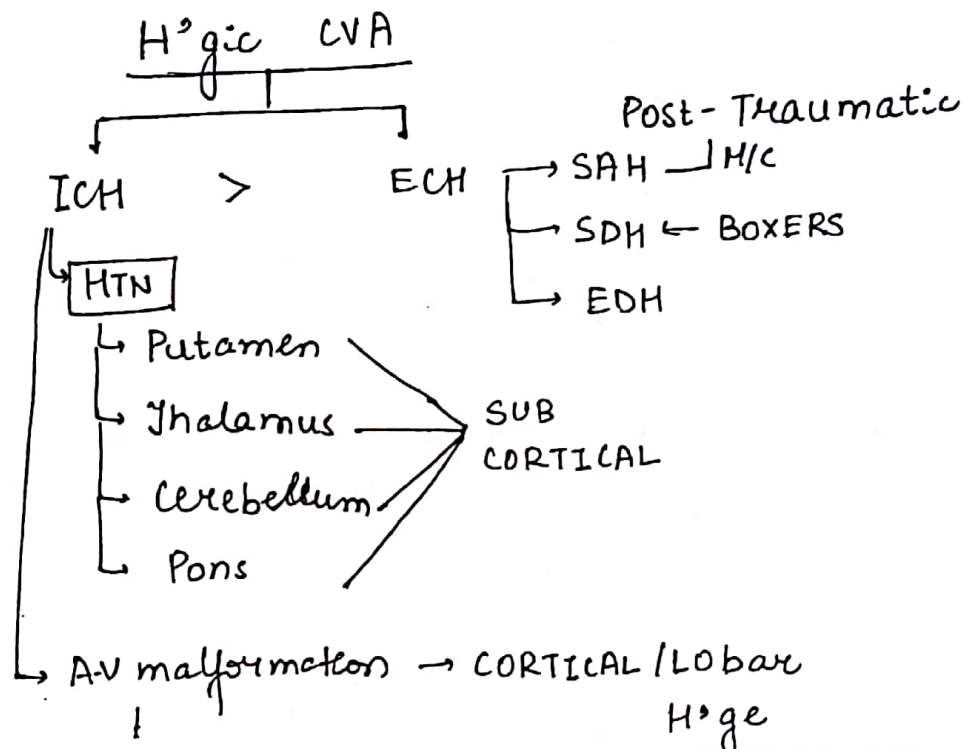
CT > MRI

- Acute = HYPER-DENSE
- Subacute = ISODENSE
- Chronic = HYPO-DENSE

MRI > CT

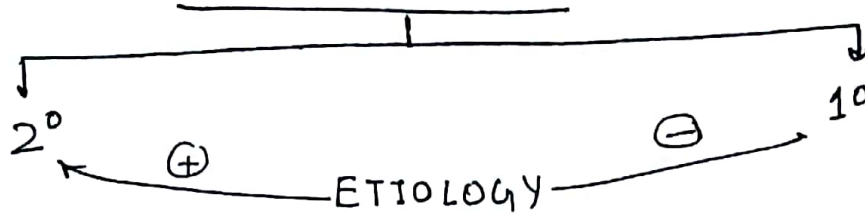
327

LUCID INTERVAL = **EDH**



HEADACHE

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TEMPORAL ARTERITIS

Elderly

♀ > ♂

Headache ⇒ Throbbing
stabbing

Scalp Tenderness → touching inflamed artery

Jaw claudication [SPECIFIC]

↳ Difficulty in chewing food

Blindness ← irreversible

↳ due to involvement of post cerebral artery

Inv-

↑ ESR

• Biopsy → Temporal Artery Biopsy
↓
Giant cells

Rx- DOC = STEROIDS

PSEUDO TUMOUR CEREBRI / BENIGN IDIOPATHIC
INTRACRANIAL HTN

M/c- young obese, ♀

Headache

Projectile vomiting (nausea \ominus)

Papulosedema

ventricle size (N)

NO focal neurological Deficit

↓ CSF Absorption.

ETIOLOGY-

- 1) Hypervitaminosis A
- 2) Expired Tetracycline
- 3) OCP
- 4) Steroid withdrawal (Abrupt)

M/C/C
↓
Idiopathic

$R_x = \text{ACETAZOLAMIDE}$
↓ CSF formation.

TENSION HEADACHE

$$f > \sigma$$

M/c 1^o Headache = Tension Headache

Associated \bar{v} DEPRESSION

Tension is not an etiology

Dull Aching Pain
Band like



R_x ↗ EPISODIC → < 15 day/mnth = ANALGESICS
↘ CHRONIC → > 15 day/mnth = T.C.A.
 ↓
 Amytryptiline

R_{xc}

MIGRAINE

330

♀ > ♂
+
4-72 hours

≥ 2 $\left\{ \begin{array}{l} P \rightarrow \text{Pulsatile} \\ U \rightarrow \text{U/L} \\ M \rightarrow \text{Moderate to Severe in Intensity} \\ A \rightarrow \text{Aggravation} \end{array} \right.$

+ any 1 $\left\{ \begin{array}{l} \text{nausea (M.C.)} \\ \text{Vomiting} \end{array} \right.$

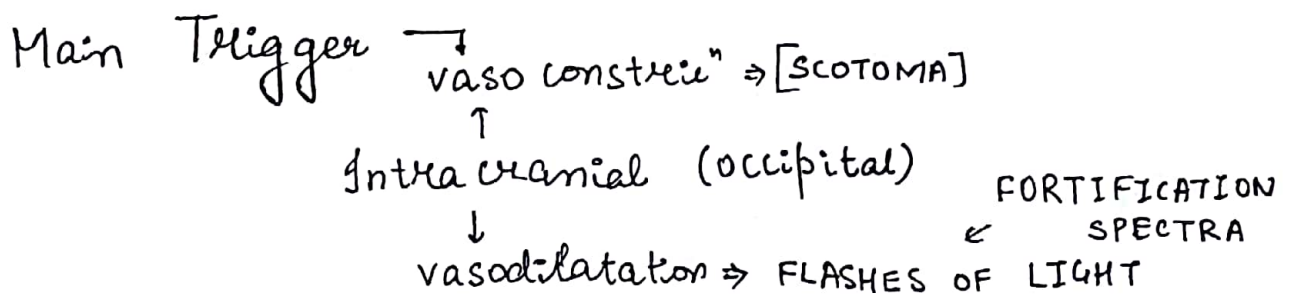
or any 1 $\left\{ \begin{array}{l} \text{Photophobia} \\ \text{Phonophobia} \end{array} \right.$

AURA = visual > sensory



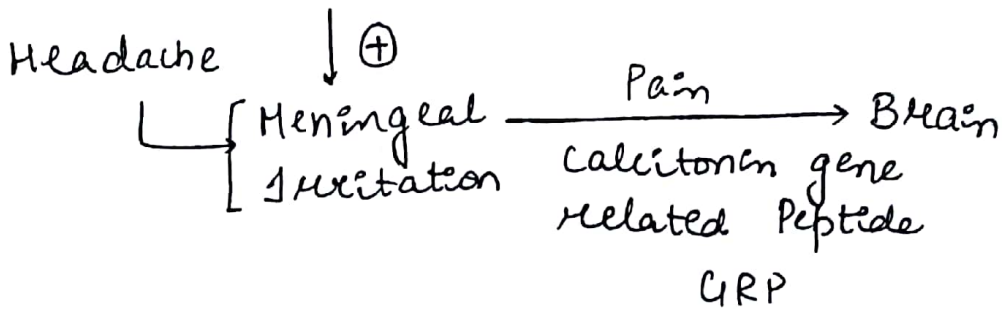
ACCEPTED THEORY

① Cortical Spreading Dissociation



vasodilation

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II SEROTONINERGIC

[5HT \ominus] \Rightarrow Throbbing

R_x = 5HT \ominus

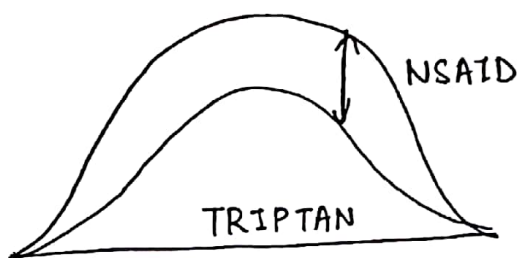
NON SELECTIVE \rightarrow ergotamine

SELECTIVE \rightarrow 1B/1D

[Triptans]

DOC for acute attack

RIZA triptan > SUMA triptan



III DOPAMINERGIC \rightarrow DA \ominus

DA \oplus \rightarrow nausea

Metoclopramide

PROPHYLAXIS x 5-6 months

① $\beta \ominus \Rightarrow$ Propranolol (widely used)

② TCA \Rightarrow Amitriptyline

③ CLB → Flunarizine

332

④ A.E.D. → Valproate
Topiramate
Gabapentine

Ethosuximide
↓
NOT Recommended.

CLUSTER HEADACHE

♂ > ♀

Peri / Retro orbital Pain

- └ U/L
- └ 30 min - 2 hours
- └ ...
- └ ppt. by consumption of alcohol
- └ awakens from sleep.

Autonomic (+)
hyperactivity

└ Lacrimation
└ Rhinorrhoea

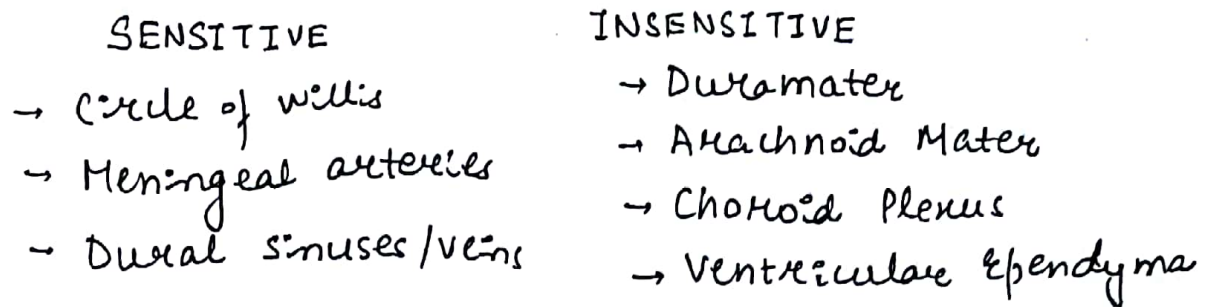
Rx = O₂ inhalation (Roc)

@ 10-12 L/min × 10-15 min

Prophylaxis = Venlafaxine (Doc)
(lifelong)

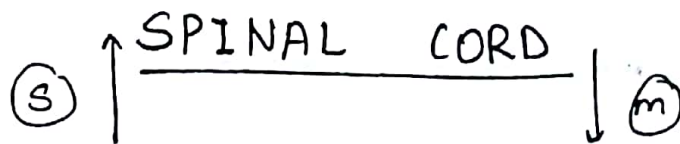
PAIN

333



DD of MIGRAINE

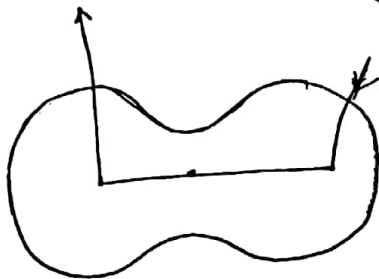
1) Glaucoma



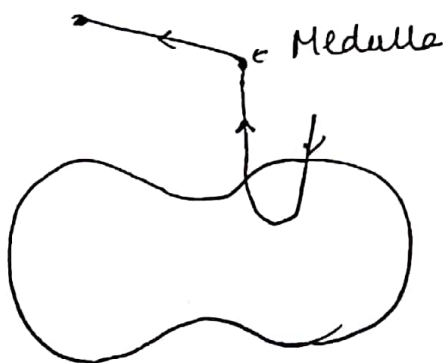
334

ASCENDING / SENSORY

SPINOTHALAMIC → Pain
Temp
Crude Touch



POST. / DORSAL COLUMN ← vibration
← proprioception (Jt. position)
← Fine touch.



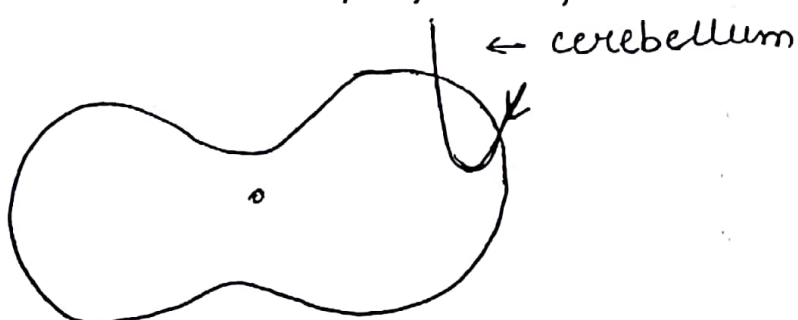
↓
LESION

↳ Stamping Gait

ROMBERG'S TEST (+) → sways & eyes closed

SPINOCEREBELLAR TRACT

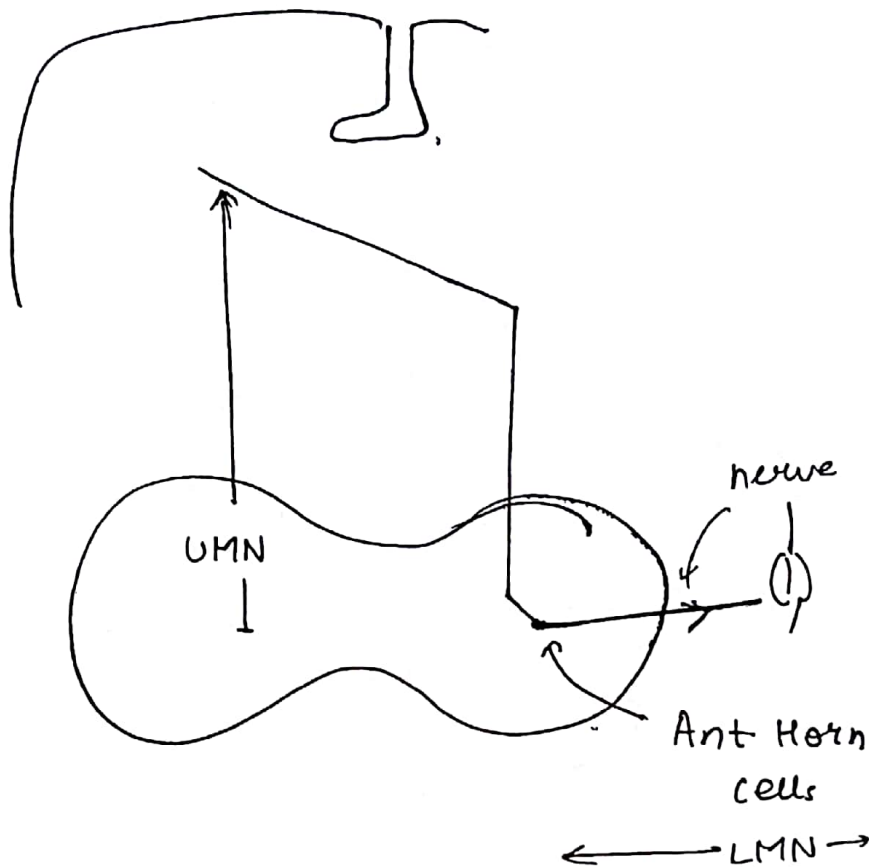
↳ Subconscious proprioception



DESCENDING TRACT

335

CORTICOSPINAL TRACT



PARALYSIS

UMN

Tone ↑ (spasticity)

DTR Brisk

Plantare extensor
[Babinski +]

LMN

↓ (flaccidity)

Dull / absent

Wasting / atrophy ⊕

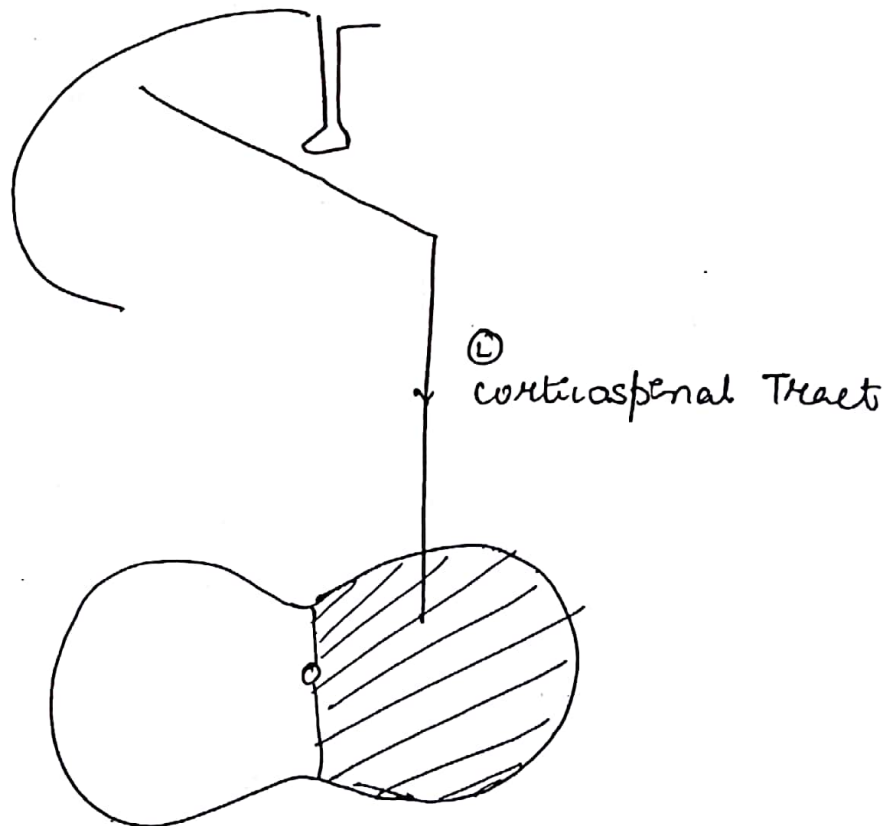
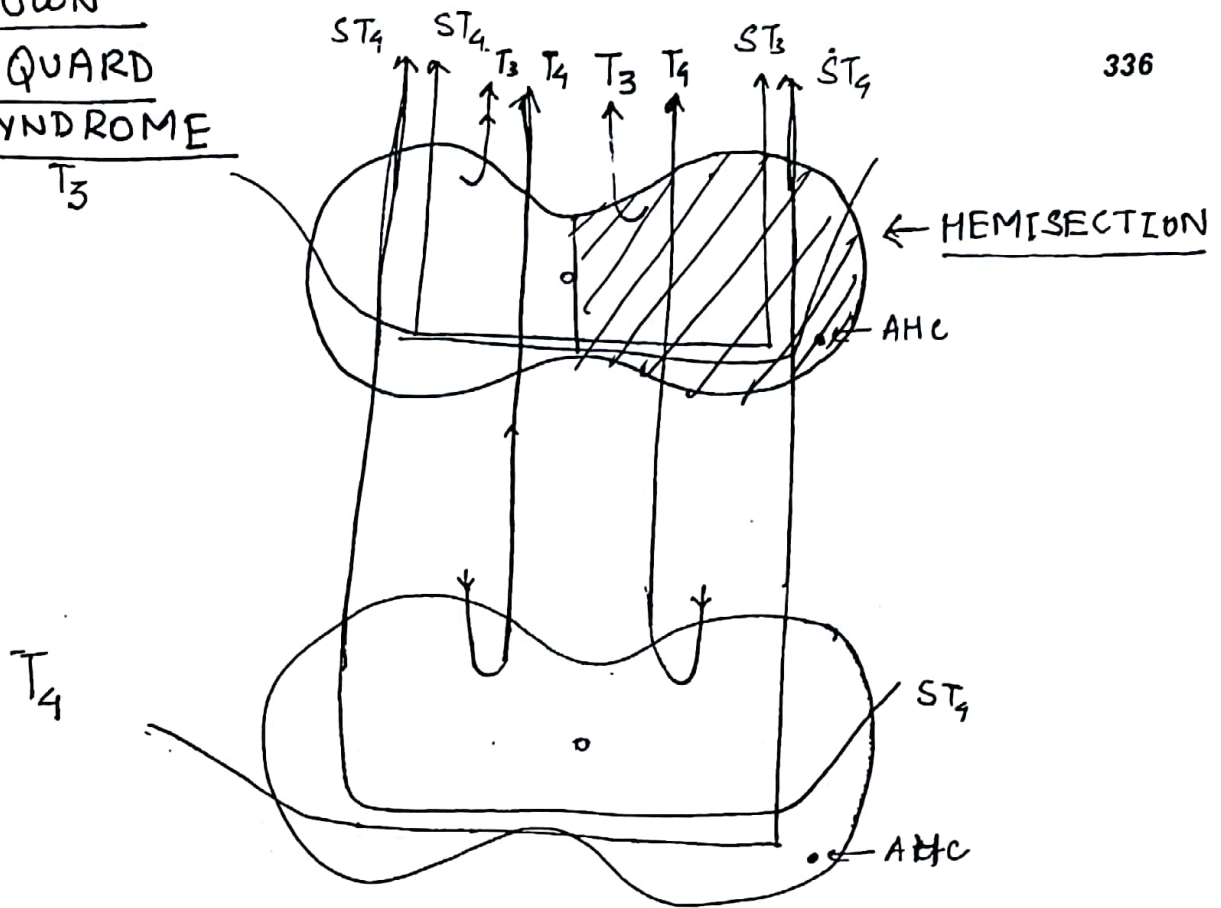
Fasciculation

↓ Twitch → visible
LESION → Palpable

↳ Ant. Horn cell.

BROWN SEQUARD SYNDROME

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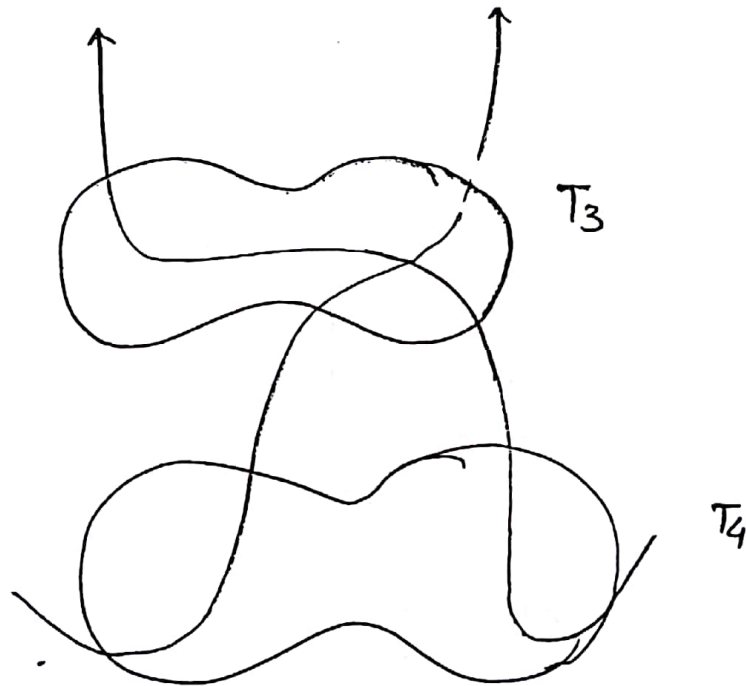
HEMISECTION of T₃

337

At T₄ → ~~CL~~ Loss of spinothalamic → C/L
Post-column → I/L
weakness → UMN
I/L.

At T_{4/3} = Loss of Post column - I/L
weakness - LMN, I/L

**** Spinothalamic - I/L ****

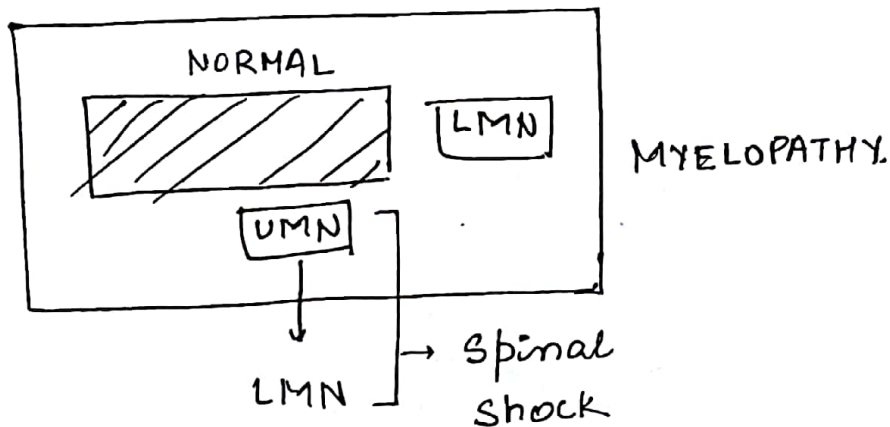
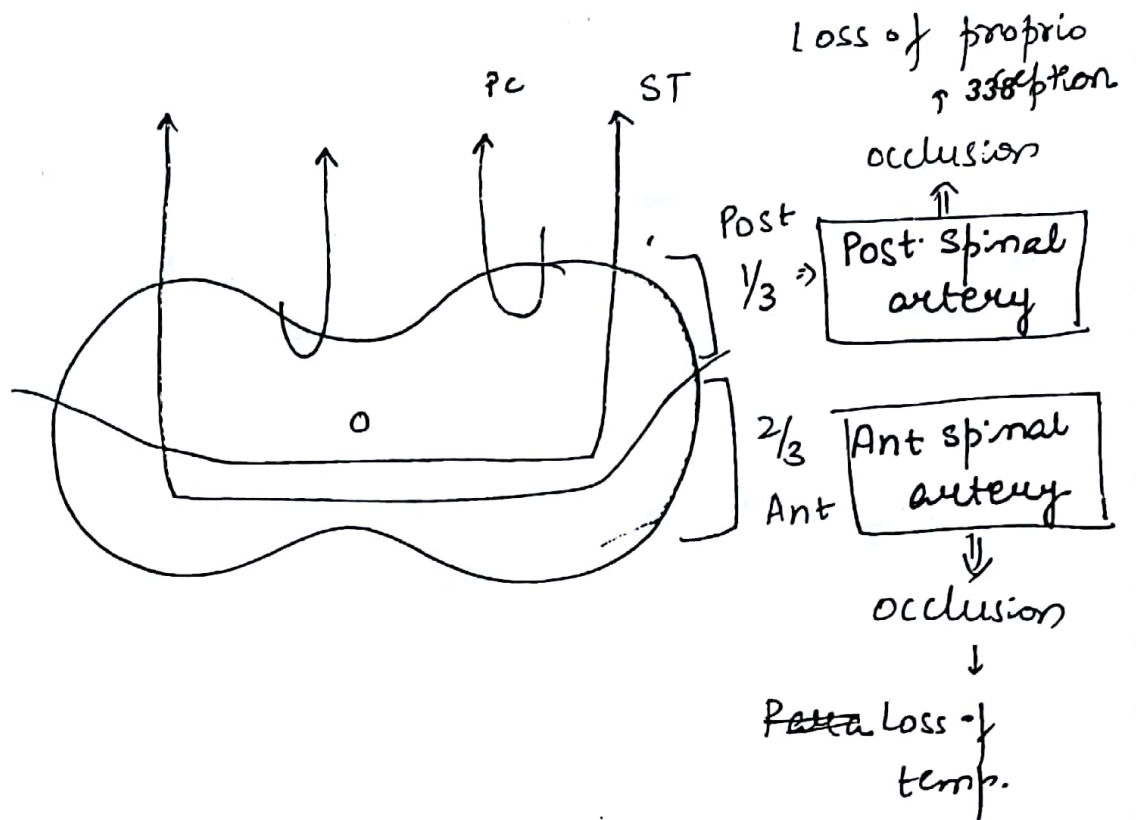


AT THE LEVEL ⇒ Spinothalamic
Post-column
LMN
SAME SIDE

~~AB~~ BELOW THE LEVEL ⇒

Spinothalamic
↓
opposite side.

P.C.
UMN
> same side



Q Q SPINAL SHOCK

Transient LMN weakness below the level of lesion

↓
most occurs

@ 48-72 hrs

- Flaccidity
- Areflexia
- urinary retention.

→ Sensory Loss

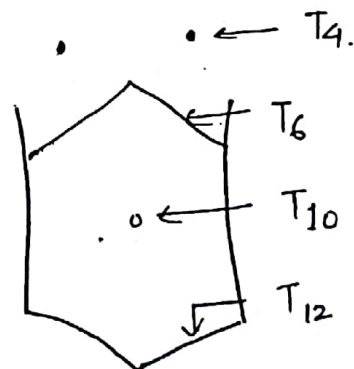
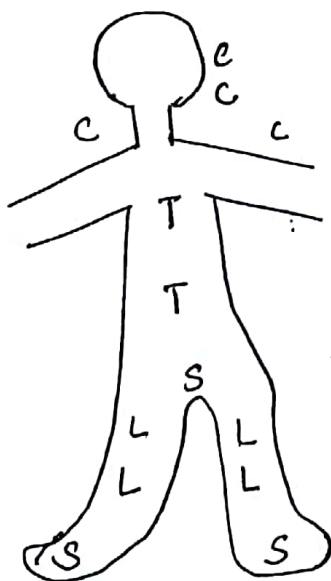
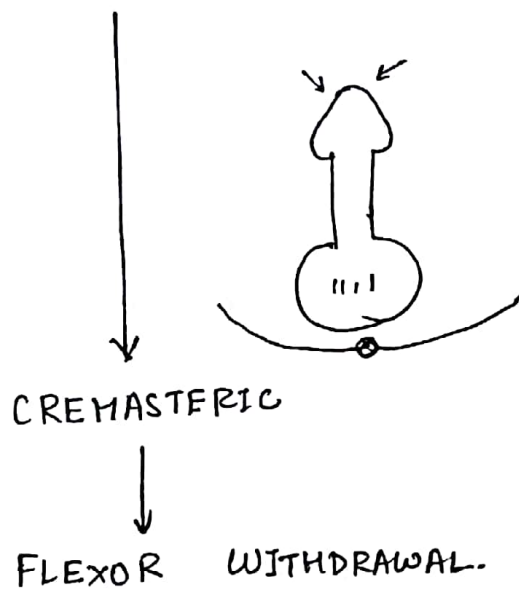
339

→ Wasting ⊖ → Transient process
internal nutrition is intact

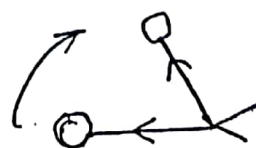
Spinal shock = LMN - wasting.

1st Reflex Recover-

BULBOCAVERNOUS. ⇒ EXTERNAL ANAL SPHINCTER.



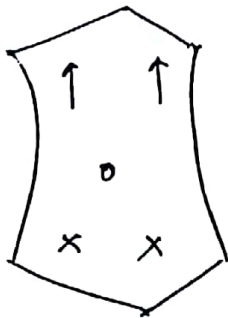
BEEVOR SIGN



BEVOR SIGN

Supine \longrightarrow sitting position

If umbilicus moves upward \Rightarrow Lesion @/below T_{10}

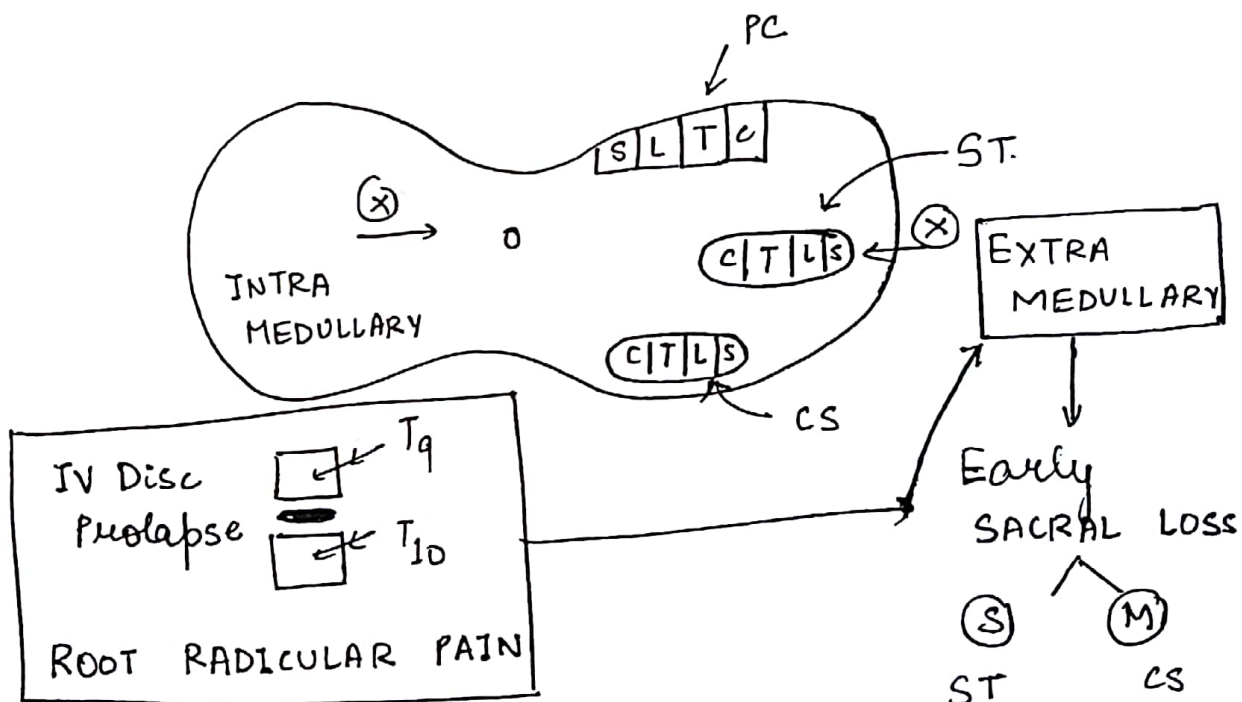


PRONATOR DRIFT SIGN

Weak side

PRONATION + ↓ DRIFT

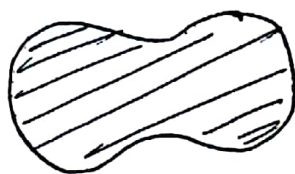
Injury CST tract
CVA In Evolution.



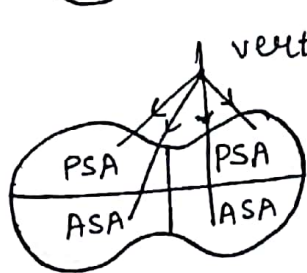
Descending $\rightarrow \begin{cases} \textcircled{S} \\ \textcircled{H} \end{cases}$ } LOSS

Burning Pain (+)

Ascending \rightarrow $\begin{matrix} \textcircled{S} \\ \textcircled{M} \end{matrix}$ } Loss

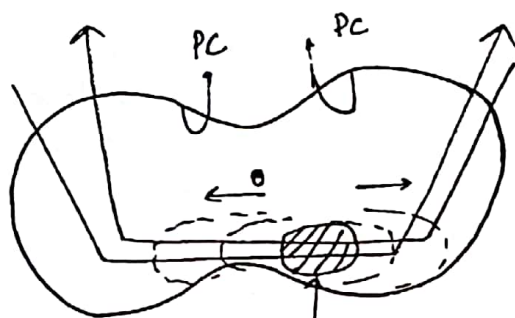


⇒ TRANSVERSE MYELITIS → extra³¹medullary
leads to
transverse
myelitis.



occlusion of 1 side ASA + PSA
↑
due to vasculitis
⇒ BROWN SEQUARD

QQ SYRINGOMYELIA



Selective Loss of
└ Pain
└ Temp

SYRINX = cavity
Assymetrical

DISSOCIATED
ANAESTHESIA

CAUSE :-

- 1) congenital
- 2) 3T
 - Trauma
 - Tumour
 - TB

M/c site

Lower cervical
upper Thoracic

AT THE LEVEL ⇒ LMN weakness

BELOW THE LEVEL ⇒ UMN weakness



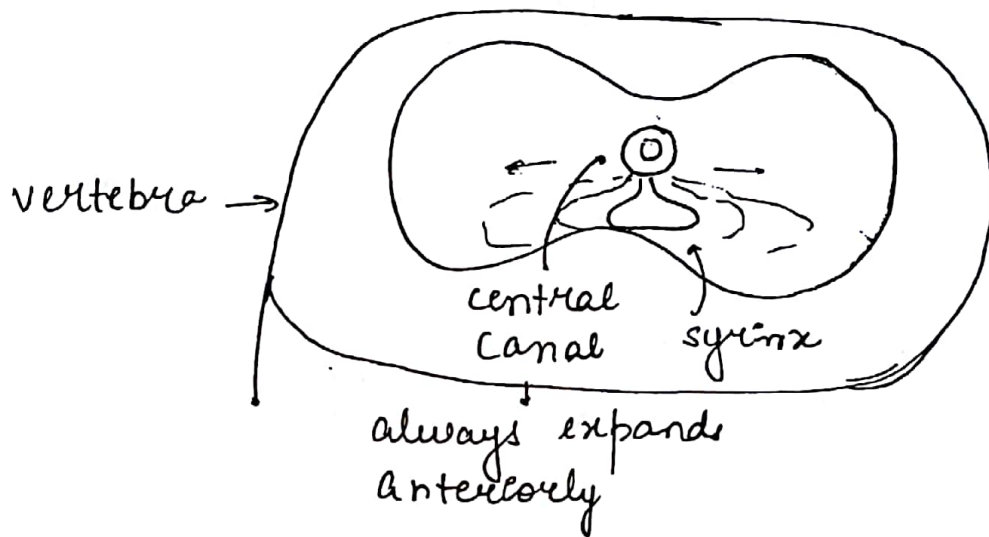
[CAPE LIKE
DISTRIBUTION OF
SENSORY LOSS]

Q/c

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CHIARI MALFORMATION > 50%
(Type 1)

⇓
Cerebellar tonsillar herniation into foramen
Magnum
↓
compresses central canal containing CSF
↓
it starts enlarging due to compression



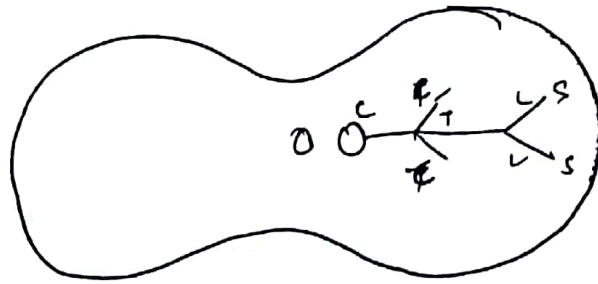
Rx = DECOMPRESSION LAMINECTOMY
| to relieve pressure on ~~the~~ expanding
| spinal cord from vertebrae

DISAD

↳ doesn't ~~a~~ relieve symptoms.

NOTES (CF of syringomyelia)

- Painless burning of hands occur early
↓
Trophic ulcers
- absent biceps jerk (C5, C6)
- extensor plantaris [L5, S1]

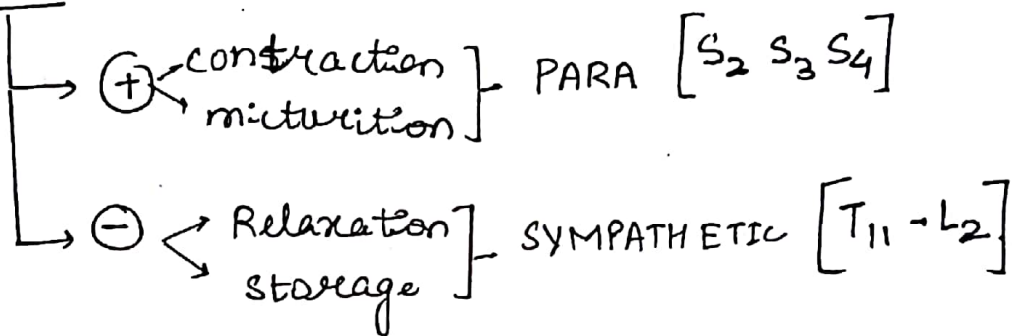


URINARY BLADDER

FRONTAL (Paracentral Lobule) where \Rightarrow ACA

PONS

CENTRE



Sensory
 S_2, S_3, S_4

[A] $S_2 S_3 S_4 \ominus$ [AUTONOMOUS BLADDER]

$S_2 S_3 S_4$

$\ominus \rightarrow$ sensory
 \rightarrow Para

$T_{11} - L_2$

++ L Sympathetic

HYPOTONIC

FLACID

LARGE CAPACITY

OVERFLOW

INCONTINENCE

[B] T₁₁-L₂ ⊖ [AUTOMATIC BLADDER]

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T₁₁-L₂

⊖ Symp

S₂, S₃, S₄

++ < sensory
parasymp

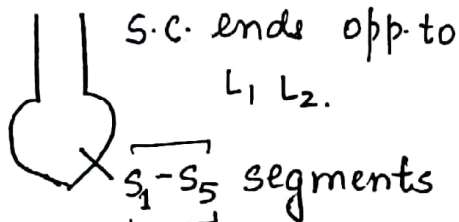
- HYPER TONIC

- SPASTIC

- LOW CAPACITY

- URGE INCONTINENCE

CONUS MEDULLARIS



KNEE JERK

L₃-L₄ ++ [N]

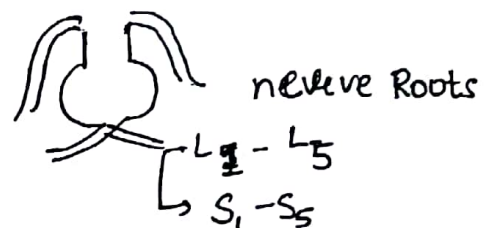
ANKLE-JERK

S₁-S₂ ⊖

BLADDER

AUTONOMOUS
(early)
Intra /

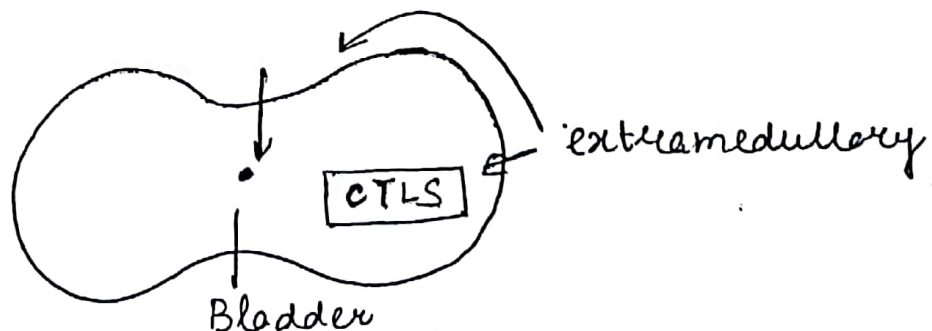
CAUDA EQUINA



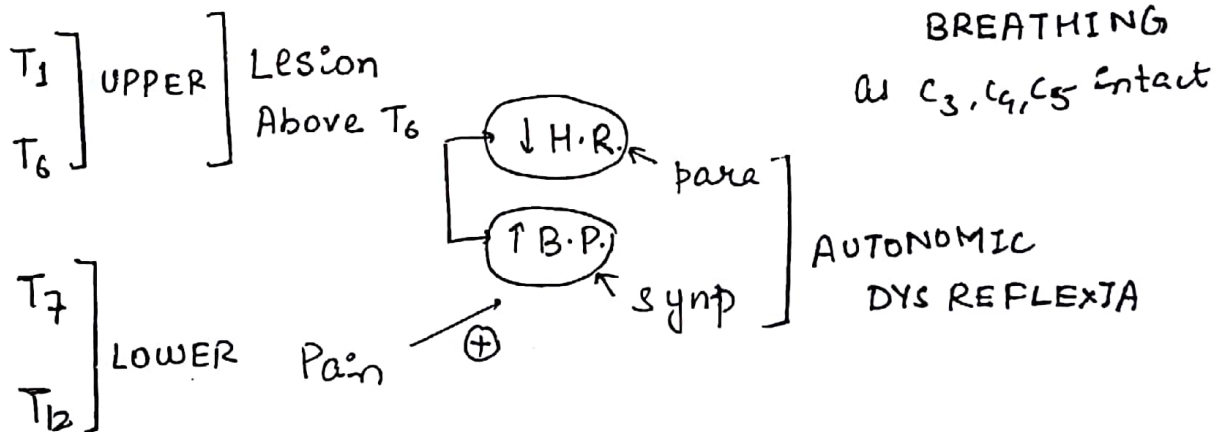
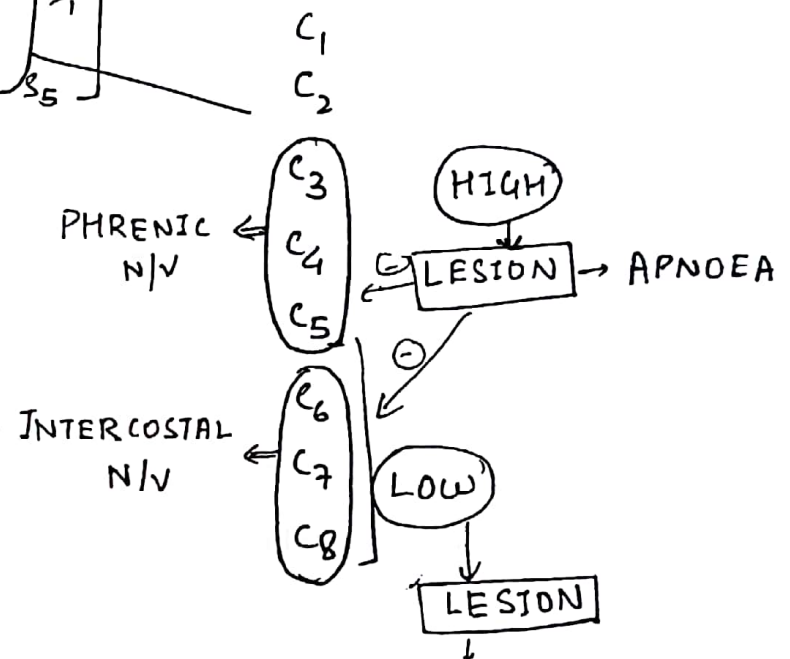
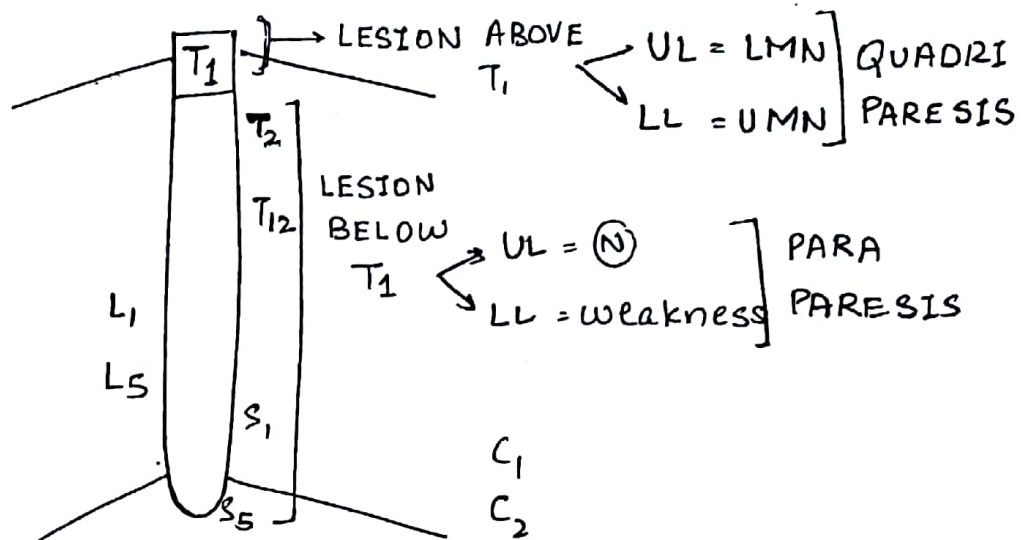
⊖

⊖

MIXED (NEUROGENIC)
(Late)
↑
Extra



Asymmetrical
Areflexic
LMN Paralysis

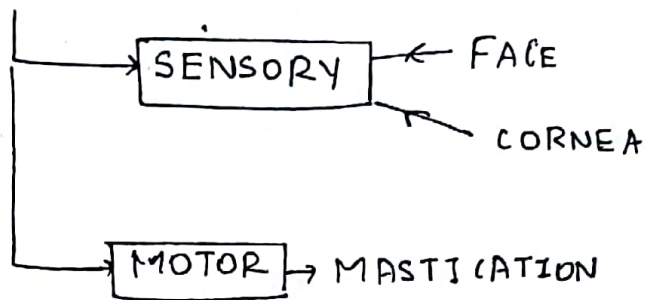


$R_x =$ NIFEDINE
CLONIDINE

TRIGEMINAL N/V

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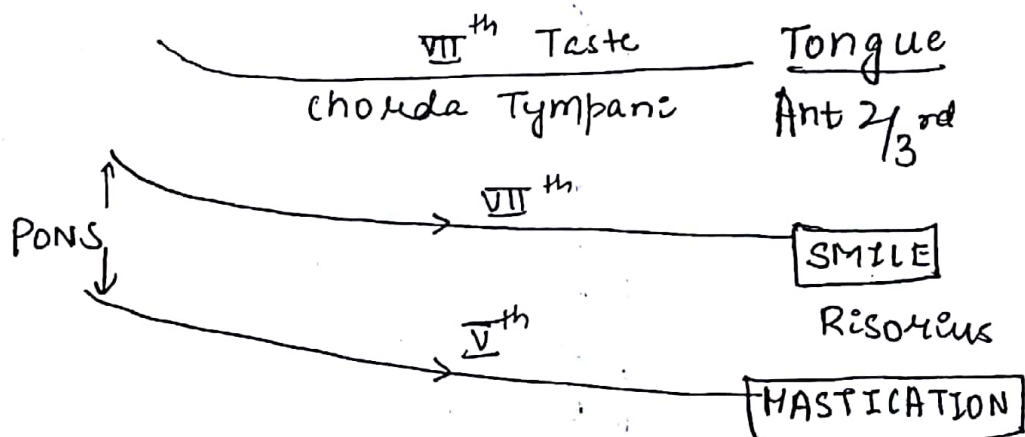
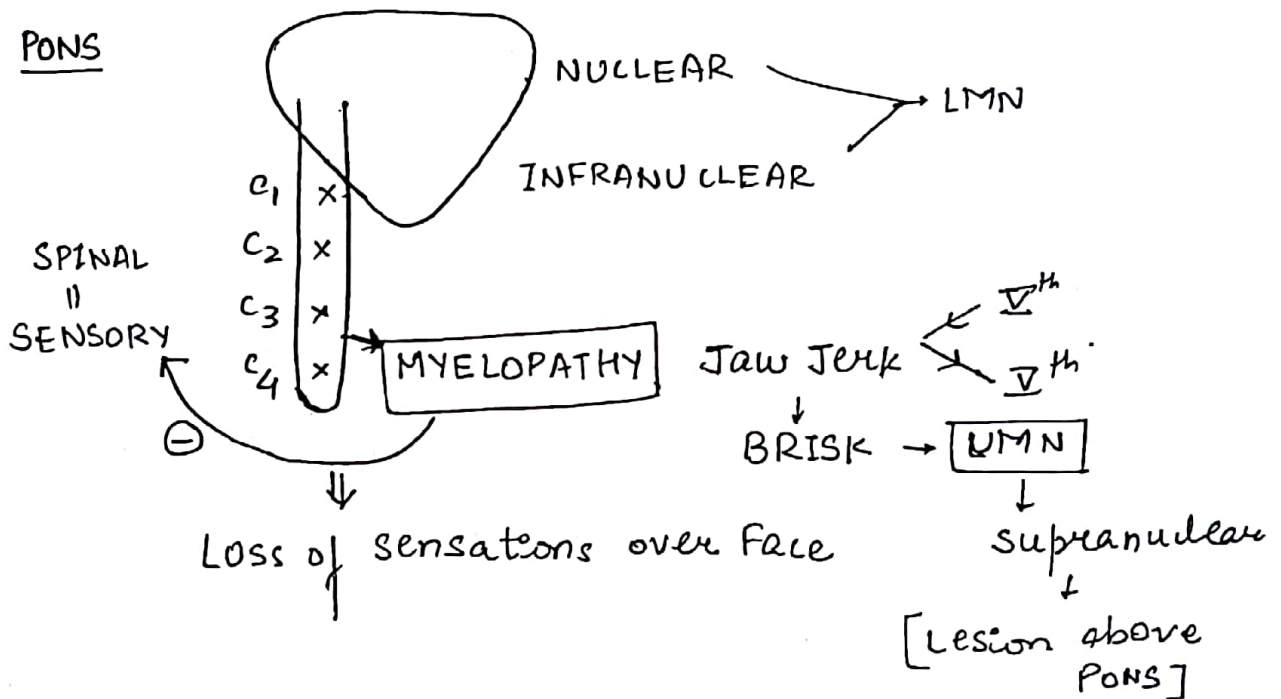
Vth N/V

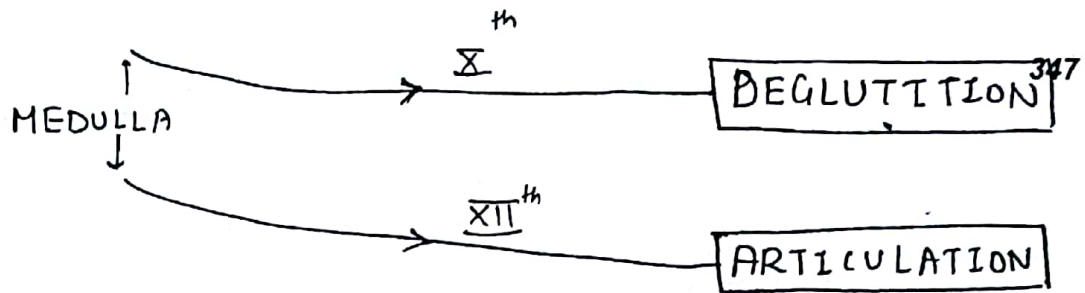


NUCLEUS

SUPRANUCLEAR → UMN

PONS





FACIAL N/V

TRIGEMINAL NEURALGIA

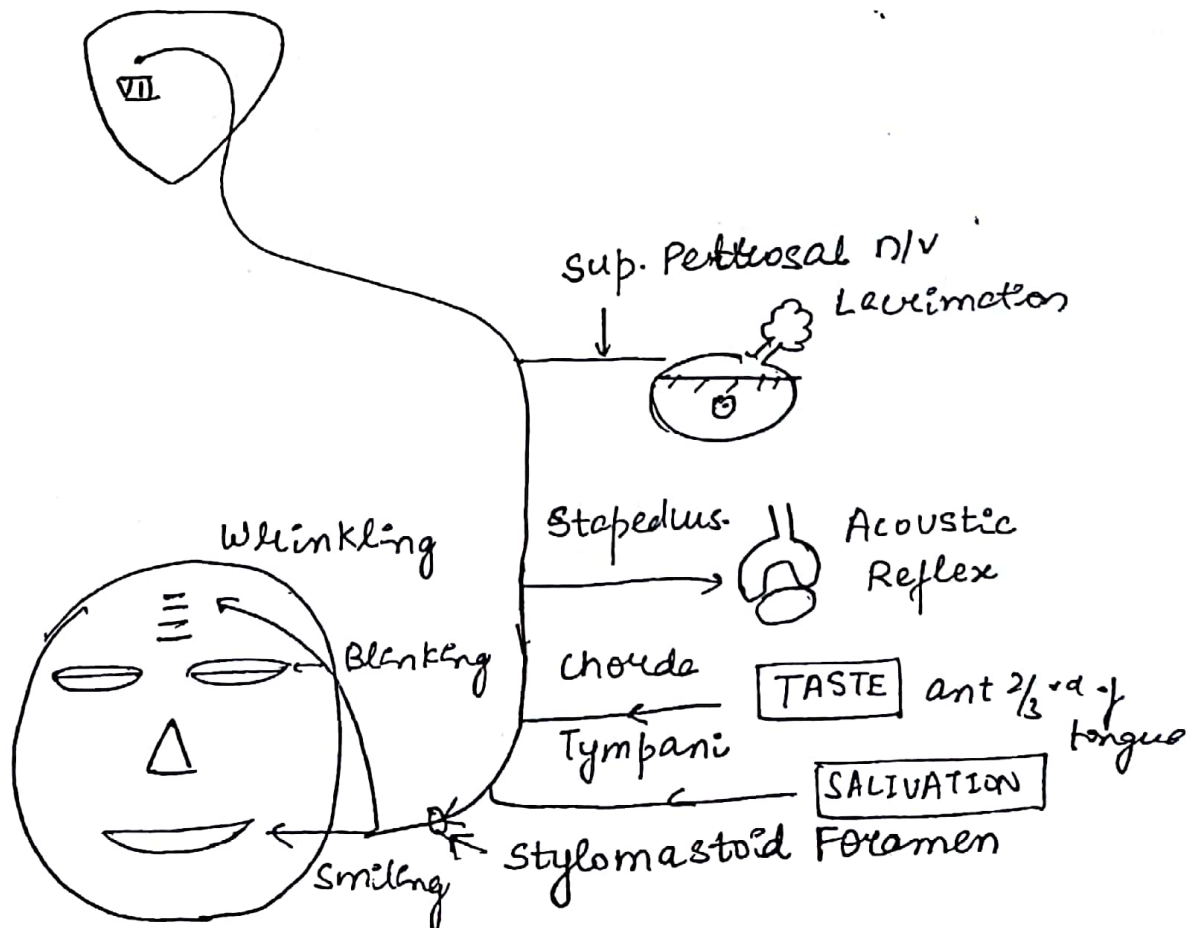
Electric shock on face / TIC DOLOREUX

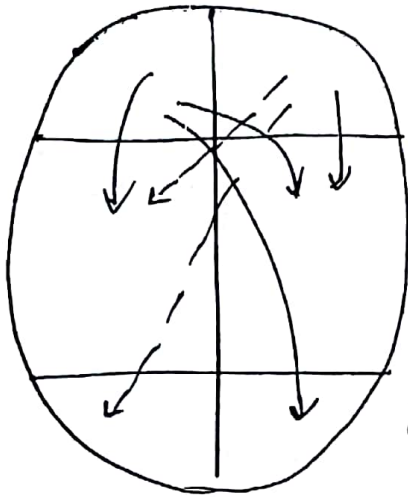
Rx → Injecⁿ of C_2H_5OH / glycerol in Gasserion ganglion

RHIZOTOMY - Radio Frequency Ablation

FACIAL N/V (VIIth)

PONS

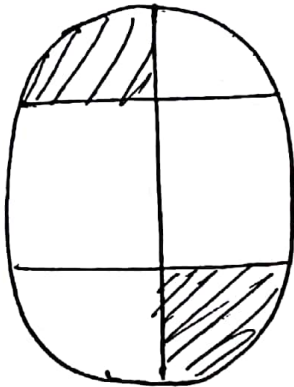




Upper $\frac{2}{3}$ rd Face is
having B/L cortical
Innervation

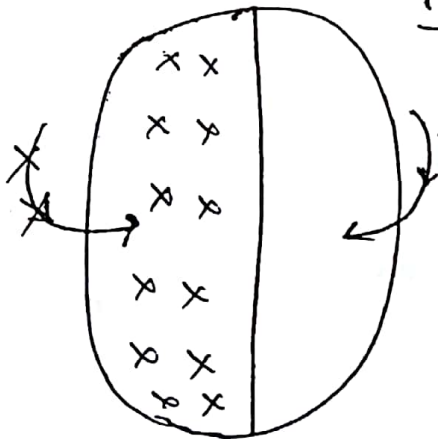
Lower $\frac{1}{3}$ rd of Face
Supplied by opposite cortex

A)



CORTICAL LESION \Rightarrow UMN PARALYSIS
(Supranuclear)

B)



PONS LESION \Rightarrow LMN PARALYSIS

U/L \rightarrow

CAUSE

- 1) Trauma
- 2) Herpes zoster virus
[RAMSAY HUNT SYNDROME]
- 3) Idiopathic [BELLS Palsy]

B/L

CAUSE

- 1) UBS
- 2) HIV
- 3) Sarcoidosis

RECOVERY

349

Abervant Reinnervation

- 1) CROCODILE TEAR SYNDROME
- 2) SYNKINESIA (smiling Blinking together)

H/O ⇒ S/O CERVICAL CORD INJURY

- 1) Fall from height
- 2) Road Traffic accident
- 3) Hanging

LHERMITTE SYMPTOM

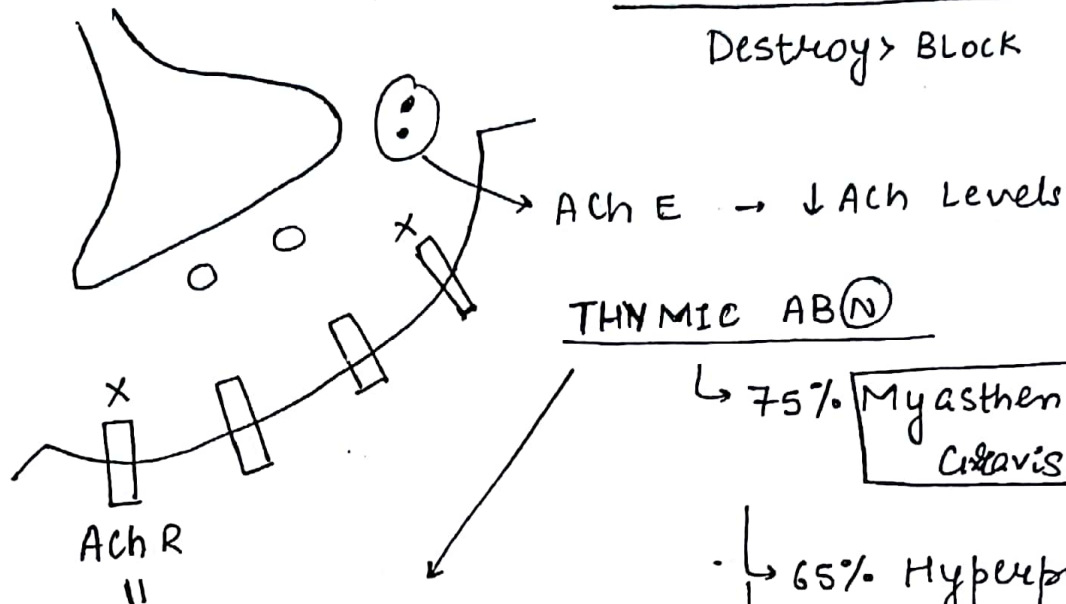
↓
MULTIPLE ON flexion of neck
SCLEROSIS. ↓
Pain / electric shock
across spine

MYASTHENIA GRAVIS

350

Ach (R) ANTIBODIES

Destroy > Block



THYMIC AB(N)

↳ 75% Myasthenia Gravis

↳ 65% Hyperplasia

↳ 10% Thymoma

Myeloid cells
↓
antigenically
mimic ACh(R)

So, Antibodies cross
React

LOCAL → Compressive

PARANEOPLASTIC

MRI
(chest)

Pure red cell Aplasia
Pernicious Anaemia
Hypo x globinemia
Dermatomyositis

♀ : ♂ = 3 : 2



3-7% MG

↓
suffer from Hypothyroidism

} So, Inv = TSH. 351

C/F :-

1> easy fatiguability

└ Proximal
└ Asymmetrical

a> OCULAR [1st m/s to involve
M/c m/s to involve]

Ptosis

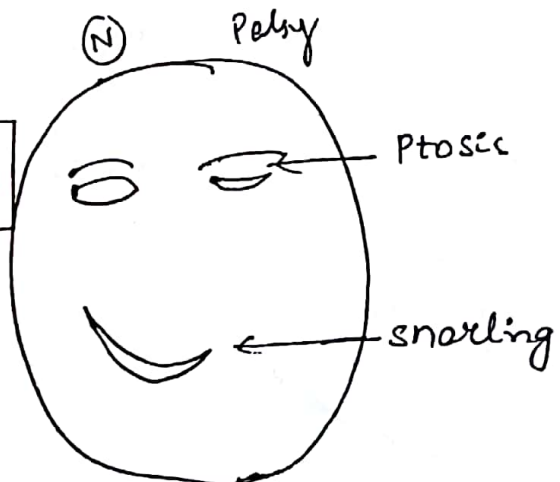
ophthalmoplegia

2) FACIAL

Snarling

↓
can't maintain
smile for long

PEEK
SIGN



close eyes for some time then
opens as if seeing through small
aperture

3> SKELETAL

(N) → DTR

└ Sensory intact
└ Bladder
└ Cognition

1> EDROPHONIUM / TENSILON TEST

↓
shorter acting
Peripheral action
[BEST SCREENING TEST]

2> ACh (R) Antibodies

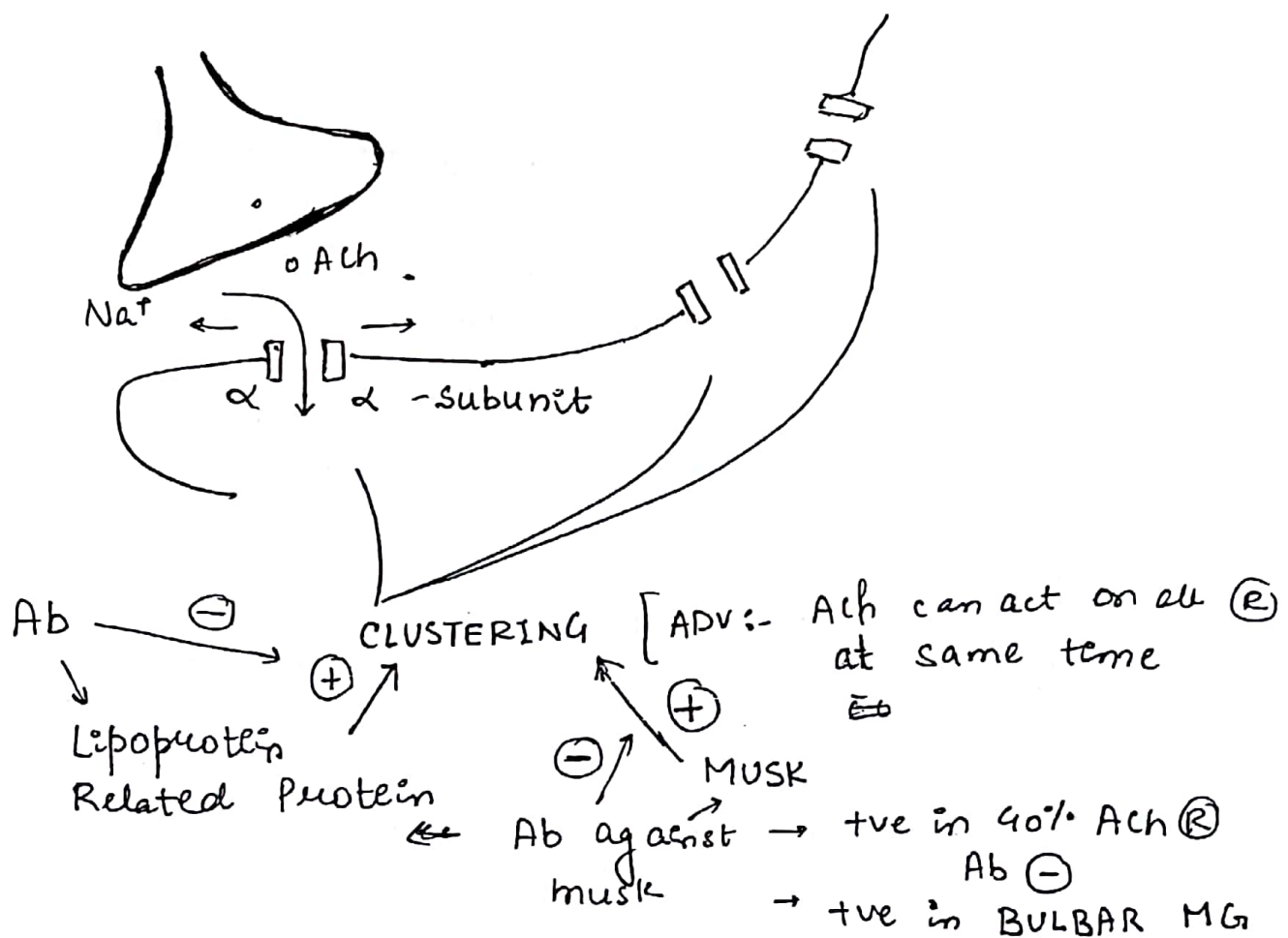
MOST SPECIFIC TEST

+ in 85% of pts. c gen. MG.
50% Ocular MG. → [eye symptoms x 3 yrs]

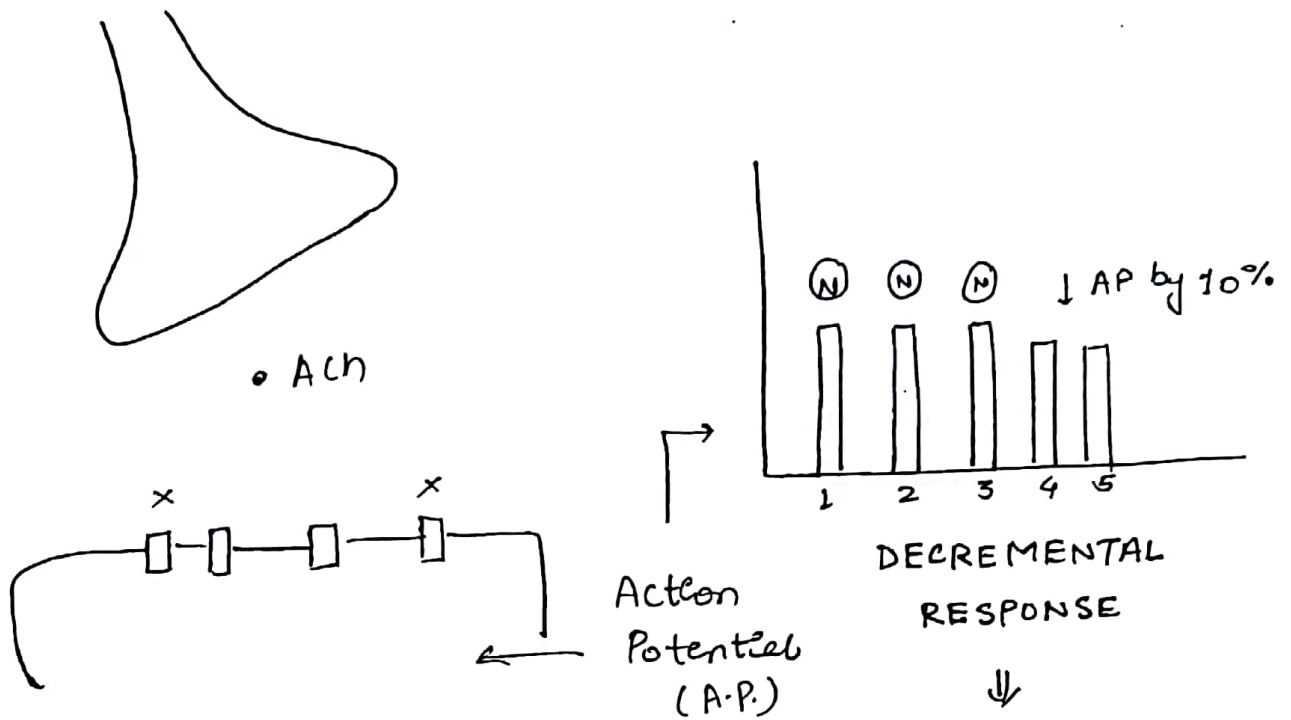
-ve doesn't rule out MG.

3> MUSCLE SPECIFIC TYROSINE KINASE (MUSK)

MUSK Antibodies

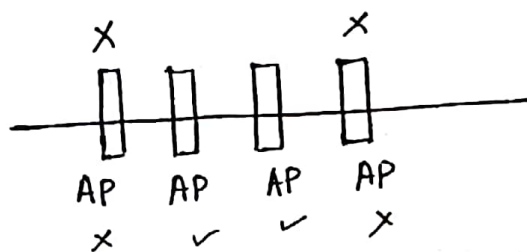


47 RAPID/REPEATED NERVE STIMULATION (RNS) 353



5> SINGLE FIBRE EMG (SFEMG) S/O MG.

↑
MOST SENSITIVE TEST
CONFIRMATORY
GOLD STD. TEST.



Difference in AP. \Rightarrow JITTER \uparrow .

↑
EMG \rightarrow shows myopathic pattern
doesn't record jitter well.

BEST

SFEMG > EDROPHONIUM > RNS

Rx

354

1> AChE ⊖

DOC → PYRIDOSTIGMINE
ACh ↑
Oral

NEOSTIGMINE
ACh ↑↑↑
Cholinergic crisis
Injectable

2> IMMUNOSUPPRESSANTS

MYCOPHENOLATE MOFETIL (MMF) — Best

3> IVIg
4> Plasmapheresis] → Refractory MG
Myasthenic crisis
↳ resp m/s weakness
↑?
Infection.

5> THYMECTOMY

35% MG → Drug Free

85% MG → Symptom Remission

It is Recommended In spite of medical.
control. [15-55yrs] [MUSK Ab ⊖]

MOST USEFUL → In Thymoma pts.
↳ local effect
↳ Paraneoplastic synd.

NOT USEFUL IN <15 yrs
↓
Immuno
Def.

>55yrs
↓
Vestigial

→ Ocular MG

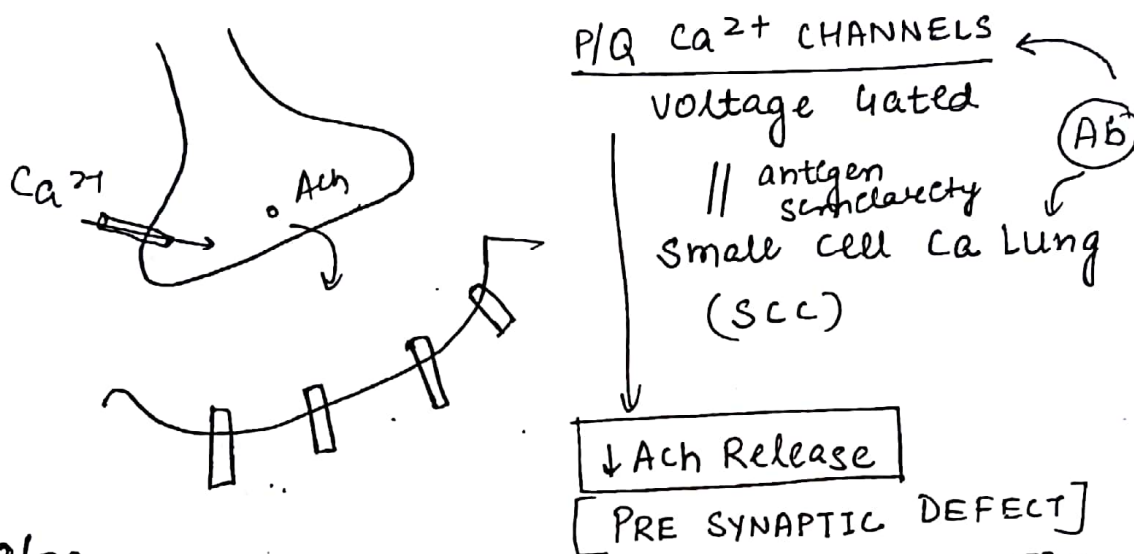
355

→ Risk surgery >> Disease

- MUSK Ab (+) [↓ Benefit]

LAMBERTEN
[LEMS]

EATON MYASTHENIC SYNDROME
[PARANEOPLASTIC SYNDROME]



C/F:-

Weakness skeletal > Facial > Ocular [MG ^{NOTE} opp. seq.]

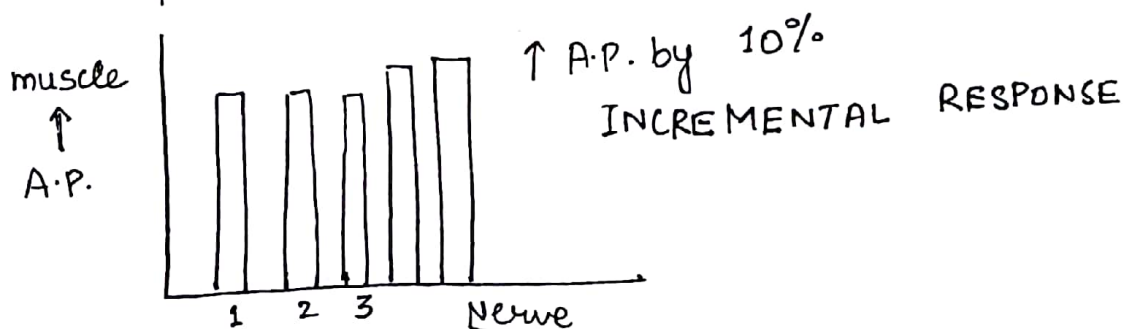
DTR ↓ / ⊖ [MG, DTR ⊕]

Bladder Involved [MG, Bladder ⊕]

INV:-

1) Edrophonium +ve. (weakly +ve compared to MG)

2) Rapid N/V stimulation Test

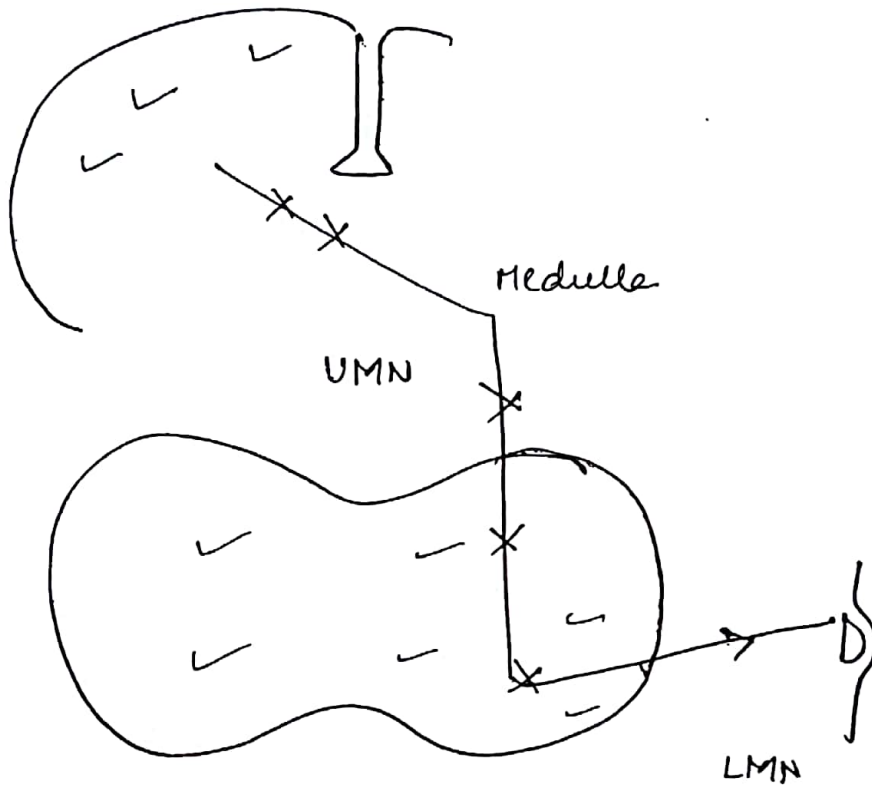


Rx -

356

↳ 3,4-Diaminopyridine \leftarrow DOC
3DAP [TACh Release]

MOTOR NEURON DISEASE



① AMYOTROPHIC LATERAL SCLEROSIS (M/L)

cortico \leftarrow UMN \equiv LMN \leftarrow due to ALS
spinal
Tract weakness is starts distally.

Amyotrophic \Rightarrow no trophic factors
weakness occurs.

II 1° LATERAL SCLEROSIS (PLS)

357

Degeneration of CS Tract \Rightarrow UMN

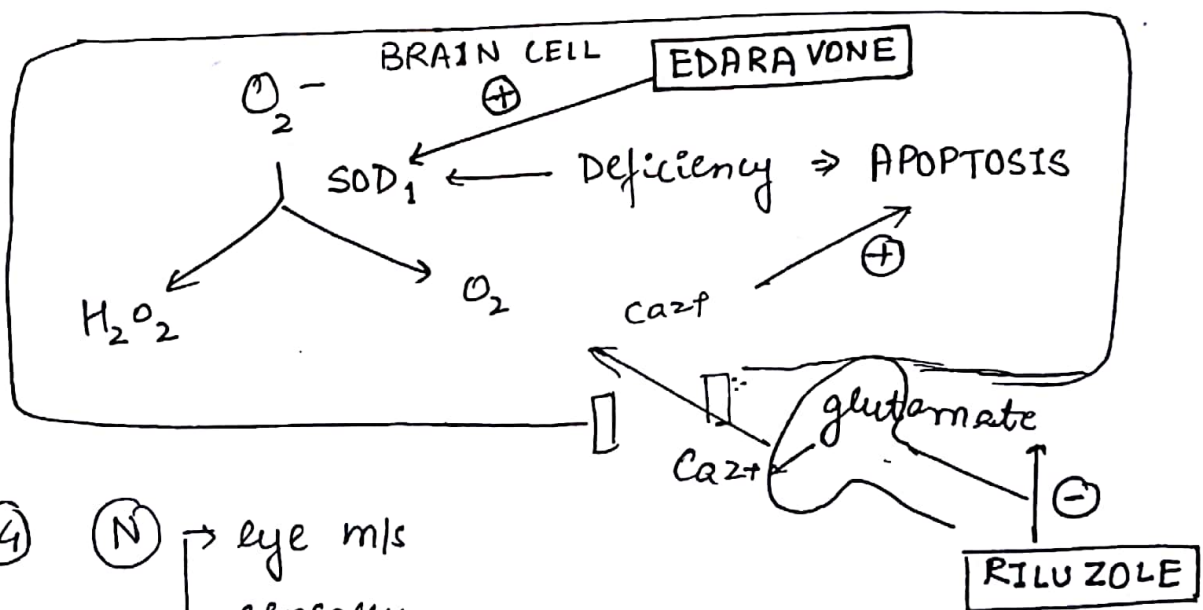
III SPINAL MUSCULAR ATROPHY

only LMN

ALS

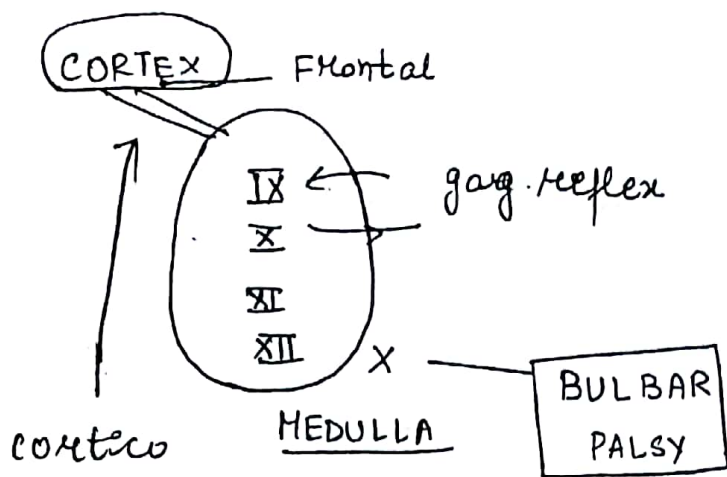
C/F -

- 1) elderly
- 2) Fasciculations \leftarrow [PATHOGNOMIC]
- 3) SUPEROXIDE DISMUTASE (SOD1) Deficiency



- ④ (N) \rightarrow eye m/s
sensory
Bladder
cognition.

⑤



PSEUDO BULBAR PALSY

Dysarthria	+
Dysphagia	+
Labile affect	+
Gag Reflex	+++

BULBAR PALSY

++

++

⊖

⊖

- ALS
- Polio
- M.G. [Bulbar MG]

ATAXIA

DRG = Dorsal Root ganglia

	FREIDRICH ATAXIA	TABES DORSALIS	SUBACUTE COMBINED DEGENERATION
<u>TRACTS</u>	POST. Pyramidal Spino cerebellar	POST.	POST. Pyramidal Peripheral n/vs
<u>VIBRA- TION</u>	⊖	⊖	⊖
<u>PROPIO- CEPTION</u>			⊕
<u>PAIN, TEMP</u>	⊕	⊕	⊕
DTR.	⊖ ^{Early} DRG involved	⊕	⊕ → ⊖ neuropathy
Babinski	+ve	⊖	+ve
ASSOCIATE D C	cardiomy- opathy Optic Atrophy DM.	Syphilis ARP ⊕ Bladder disturbance	↓ vit B ₁₂ Megaloblastic Anaemia

FREIDRICH'S

Trinucleotide Repeat sequence = GAA

AR
Chr. 9

TABES DORSALIS

Syphilis.

Argyll Robertson Pupils.

Bladder Disturbance

SACB

↓ vit B₁₂.

↓
Megaloblastic
Anaemia

CEREBELLAR LESIONS

Dysmetria → Past Pointing

Titubation → persistent head nodding

Intentional Tremor

Dysdiadochokinesia

Pendular knee Jerk

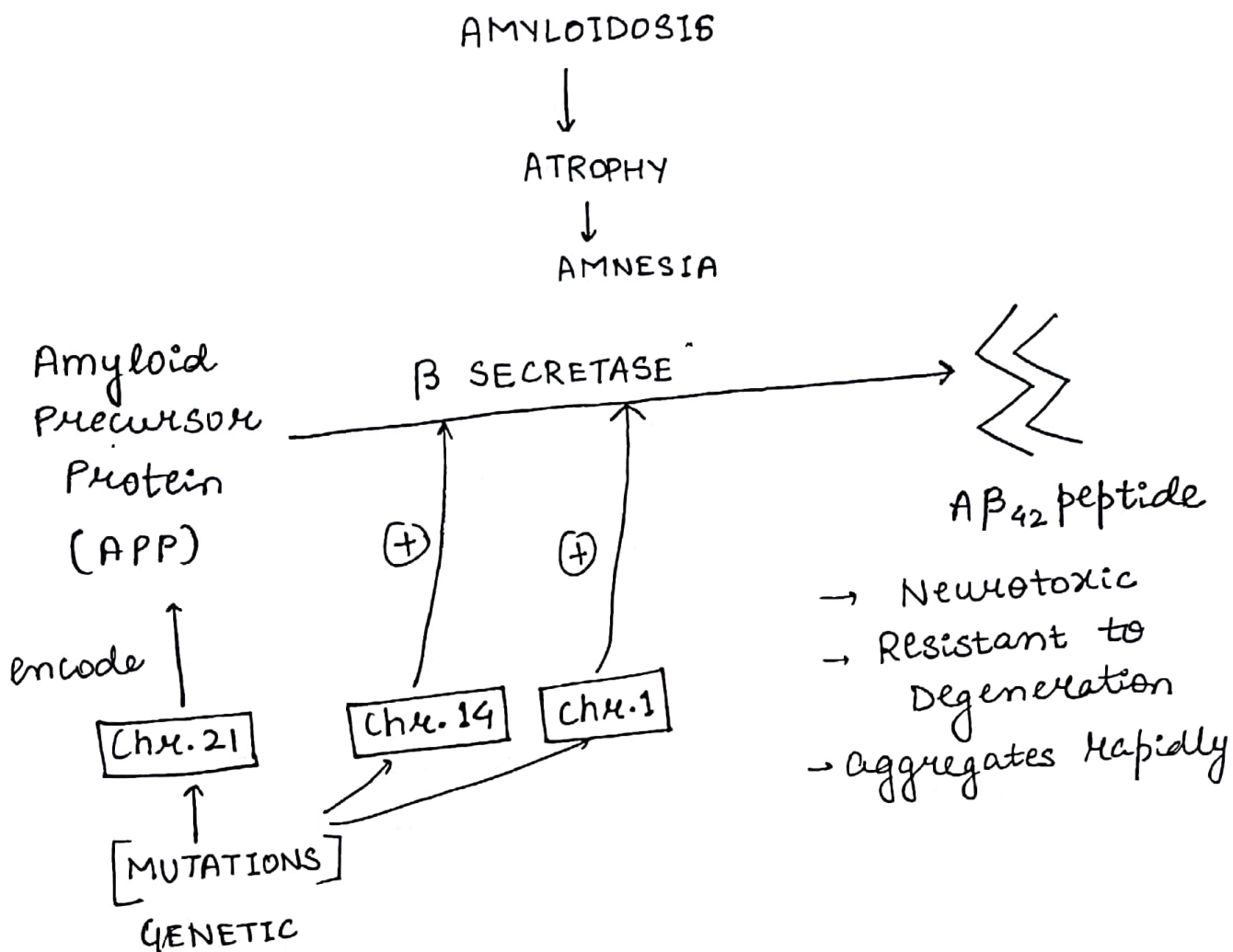
Romberg's Test (+) → Lesion in Post. column

Broad Based Gait

Tendency to fall towards Lesion.

ALZHEIMER DISEASE

361



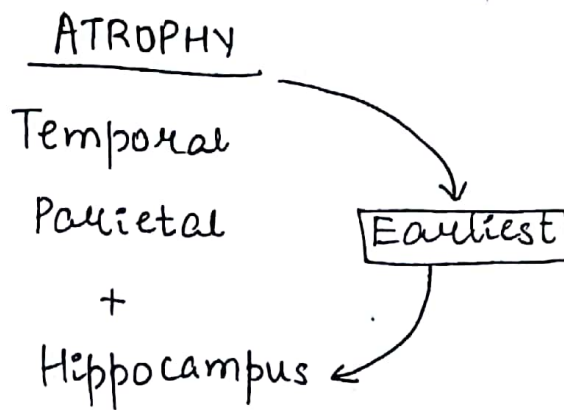
RISK

↑
Elderly
♀
Chx. 19 - Apo E₄ gene
Aluminium
Mercury
Family H/O
Low Education
(poor maths)

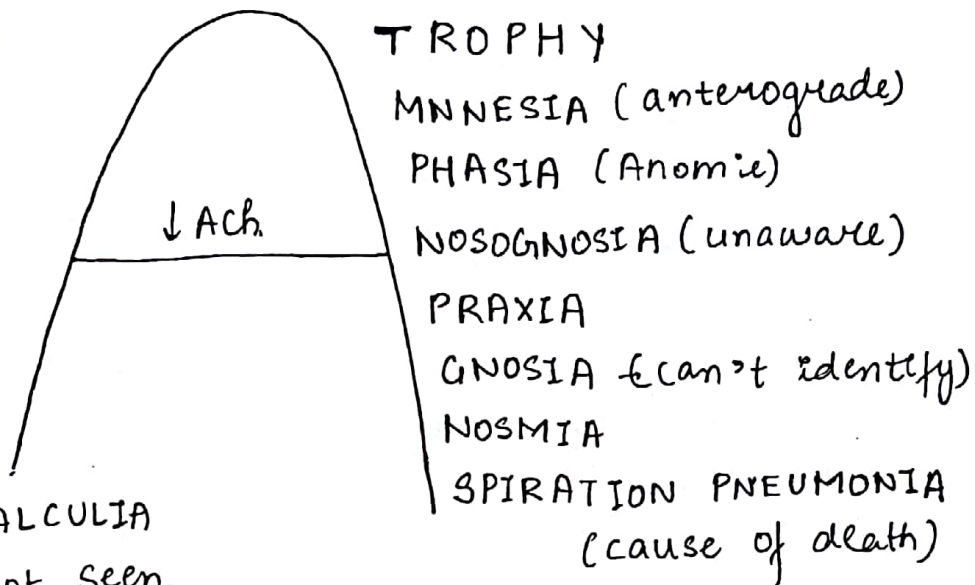
↓
Post Menopausal. Estrogen
NSAID Use

Apo E₂ gene.

Smoking
↓
Risk → Parkinsonism
 → Ulcerative colitis



C/F



→ ACALCULIA
is not seen.
[DSM CRITERIA]

→ AGNOSIA
not seen in early onset
Alzheimer's (age < 65 yrs)
[ICD CRITERIA]

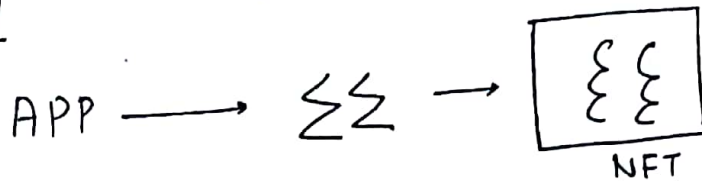
→ DELUSION (false belief)
" OF DOUBLES

→ Doctor replaced by enemy

CAPURAS Syndrome
(in 10% of pt)

BIOPSY

363



1> NEUROFIBRILLARY TRIANGLES

Intracellular

Correlate \bar{c} severity

TAU - Hyper PO_4^- microtubular proteins
s/o neurodegeneration

Also seen in TAU Pathies

1> Fronto Temporal Dementia

- Behavioural Ab^(N) due to frontal lobe involvement \rightarrow early, \rightarrow severe
- memory loss \rightarrow Late \rightarrow mild
- Age of onset < 65 yrs.
- Insight \ominus

2> Progressive Supranuclear Palsy (PSP)

- extended posture
- downward gaze $\ominus \rightarrow$ fall
- dementia

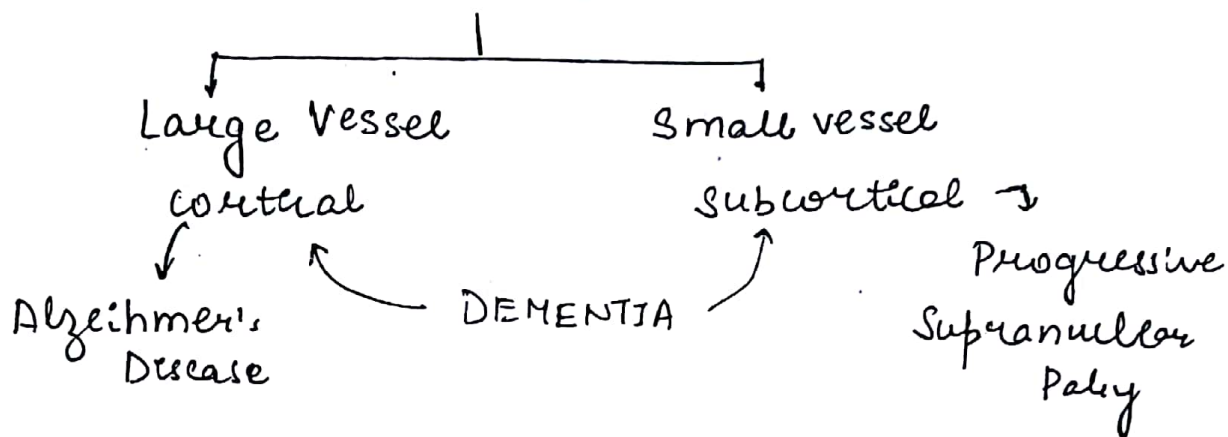
3> Corticobasilar Degeneration [PD + myoclonus + Dystonia]

27 SENILE NEURITIC PLAQUES (SNP)

364

- extracellular
- correlate \bar{c} Age

CEREBRAL AMYLOID ANGIOPATHY (CAA)



3) GRANULOVASCULAR DEGENERATION

Best seen in HIPPOCAMPUS

HUNTINGTON'S CHOREA

→ Huntington gene [Chr. 4 - short arm] Trinucleotide Repeat Sequence defect
CAG > 40 repeats.

→ AD inheritance

- ↓
- 2 successive generations are affected
- 1 Parent affected
[chance 50%] 1:2

- If Both parents affected.
[chance 75%] (3:4)

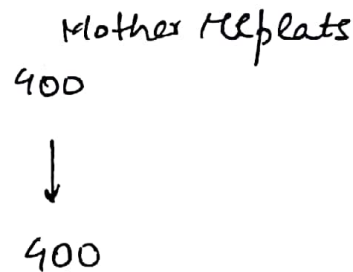
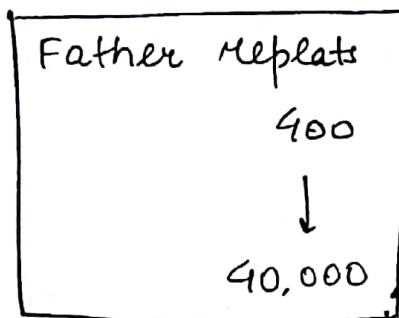
ANTICIPATION

365

(11-50 yrs) \rightarrow ♂ = early onset 2nd Decade
(Father)
 \rightarrow Mother = Late Onset 4th Decade.

LENGTHENING

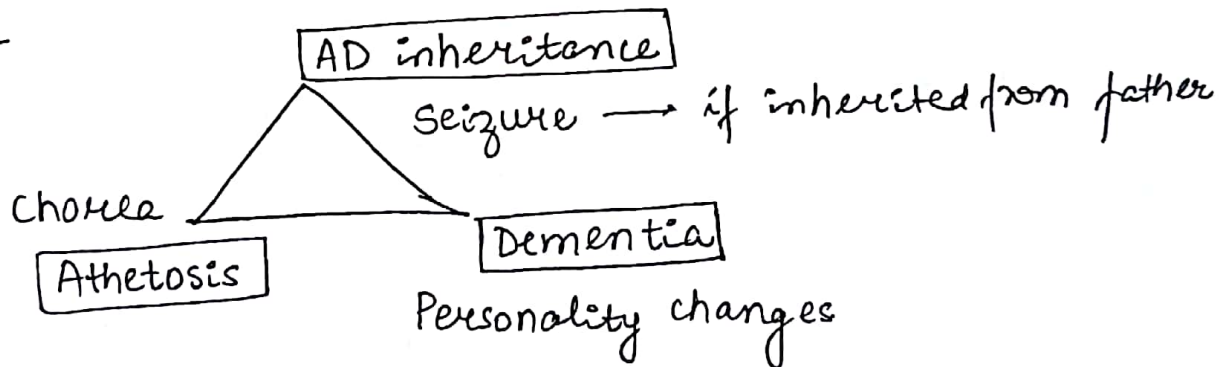
Larger Defect \rightarrow ↑ severe
 \rightarrow early onset (from father)



Anticipation

\rightarrow occurs due to lengthening

C/R -



ATROPHY \rightarrow in CAUDATE NUCLEUS.

↓ ACh ↓ GABA Intra striatal
↑ DA

Rx \rightarrow DA \ominus \rightarrow Haloperidol

DA Depletor \rightarrow Tetrabenzine \leftarrow DOC

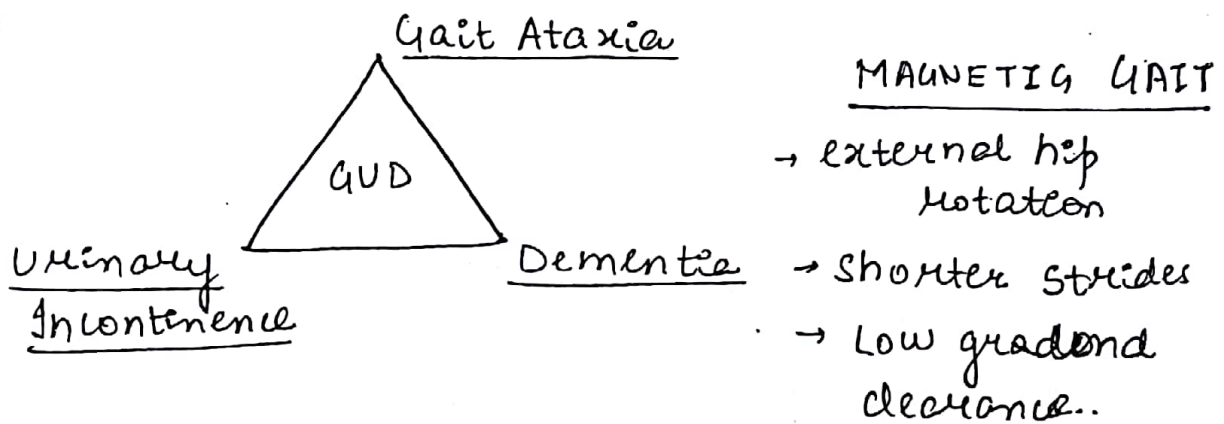
NORMAL PRESSURE HYDROCEPHALUS (NPH)

CSF PRESSURE \rightarrow (N) = 50 - 150

\downarrow NPH = 150 - 180

\downarrow CSF Absorption. \leftarrow SAH
 \uparrow Meningitis

C/F



SCISSORING GAIT \rightarrow spastic CP

CHARLIE CHAPLIN GAIT \rightarrow Tibial Torsion

Rx

V-P shunt



1st / Most responsive symptom to improve on VP shunt
ATAXIA

Q Q WERNICKE'S ENCEPHALOPATHY

367

EA PREDISPOSED -

- 1) Hyperemesis
- 2) Alcohol Intake

→ B₁ Deficiency

↓
CO-FACTOR for.

α -keto glutarate dehydrogenase
Pyruvate Dehydrogenase

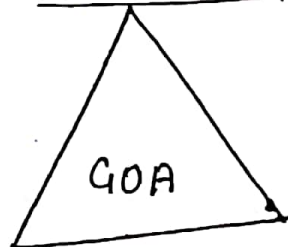
↓
GLUCOSE ACCUMULATION

↓
Mitochondrial Damage

↓
NEUROTOXIC

C/F

GLOBAL confusion



Ophthalmoplegia

Ataxia

Rx

THIAMINE REPLACEMENT x 14 Days.
(100 mg/day)

1st Improve = ophthalmoplegia

[Glucose Infusion can Precipitate it]

KORSAKOFF'S PSYCHOSIS / ALCOHOL DEMENTIA ³⁶⁸

DEMENTIA → CONFABULATION
False story to hide
memory loss

SITES

Periaqueductal Grey Matter

Mamillary Bodies

Thalamus → [AMNESTIC DEFECT]

CONFUSIONAL STATE

- 1) seizure
- 2) T.I.A.
- 3) Metabolic → ↓ glucose
↳ alcohol

TRANSIENT GLOBAL AMNESIA

Both anterograde + Retrograde amnesia

CNS INFECTIONS

369

BACTERIAL / PYOGENIC MENINGITIDES

M/C/C

(Epidemic)

Adolescent / Adult = N-MENINGITIDIS

Elderly = STEPTO-PNEUMONIA
(Community acquired)

CSF

ⓐ appearance

Ⓝ

PYOGENIC

Appearance	Transparent	Turbid
cell count	≤ 5	Pleocytosis ($N > 76$)
Protein	15-45 mg/dL	↑↑
Glucose	40-70 mg/dL	↓↓↓
Cl ⁻	116-126 meq/L	↓ / Ⓝ

Hypoglycorrhizia = ↓ CSF Glucose

Rx

N-MENINGITIDES → Ceftriaxone x 7 Days

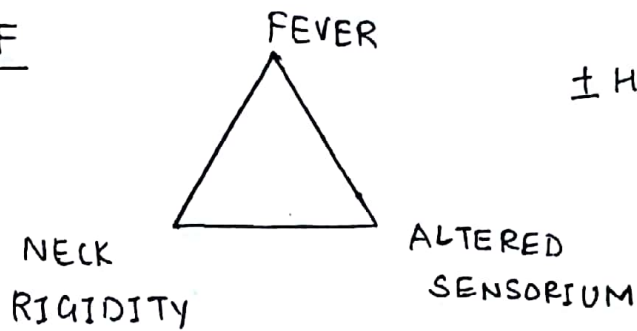
S. PNEUMONIAE

→ Ceftriaxone + vancomycin } x 14 Days

> 60 yep

↓
LISTERIA → Ampicillin

C/F



± HEADACHE.

370

Dexamethasone

10 ~~mg~~ mg IV stat

↓
1st Dose of antibiotic

TBM

M/c Meningitis in India

TBM ATT x 1 month

↓ sensorium

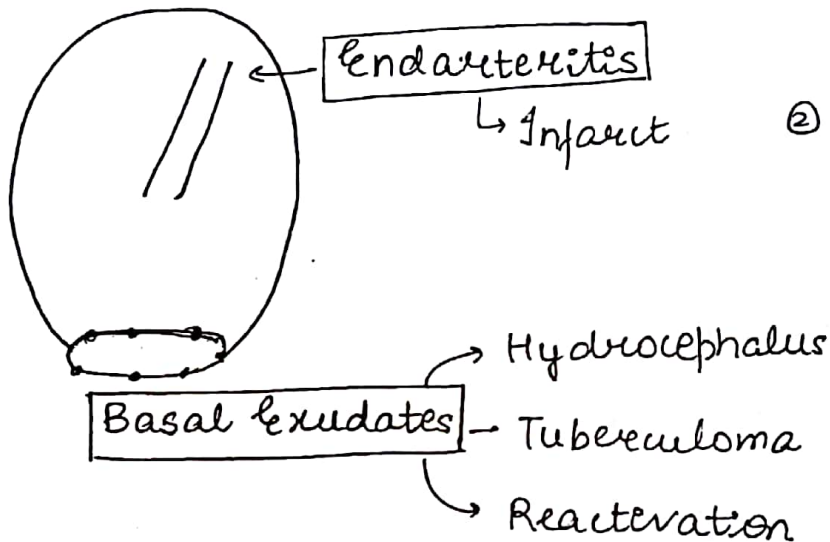
① ATT induced hepatic
↳ hepatic encephalopathy

② ↑ ICT → cerebral salt wasting


③ Infarct

④ Tuberculoma

⑤ Hydrocephalus



CSF

- 
- COB-WEB
 - Pleocytosis [L > N]
 - Protein ↑↑↑
 - Glucose ↓ Cl⁻ ↓↓↓

GOLD STD TEST = Culture of CSF

Rx

ATT x 12-18 months (↓ Reactivation)

Steroids x 2 months [⊖ Endarteritis]

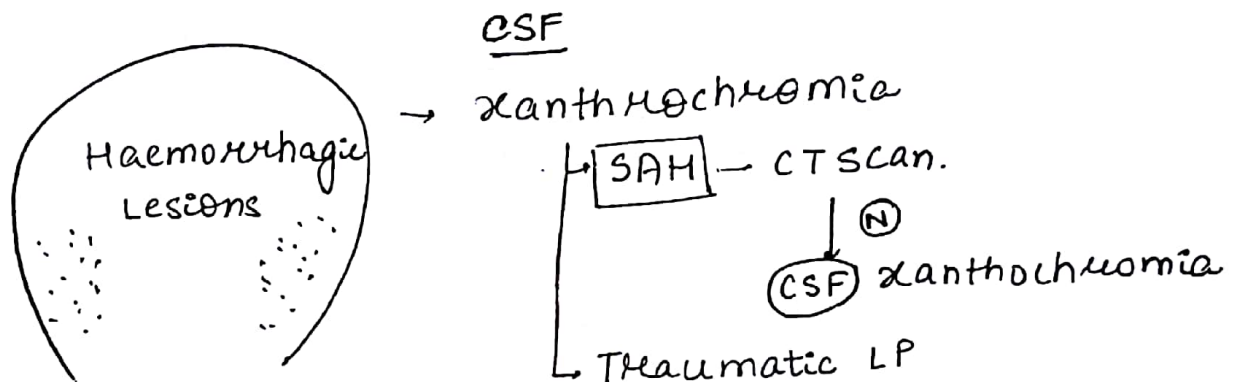
VIRAL ENCEPHALITIS

371

M/C C → ENTEROVIRUS

└ epidemic = ARBOVIRUS
└ sporadic = HSV type 1

HSV ENCEPHALITIS



- Pleocytosis
- ↑ Protein
- (N) Glucose
- Cl^- ↓

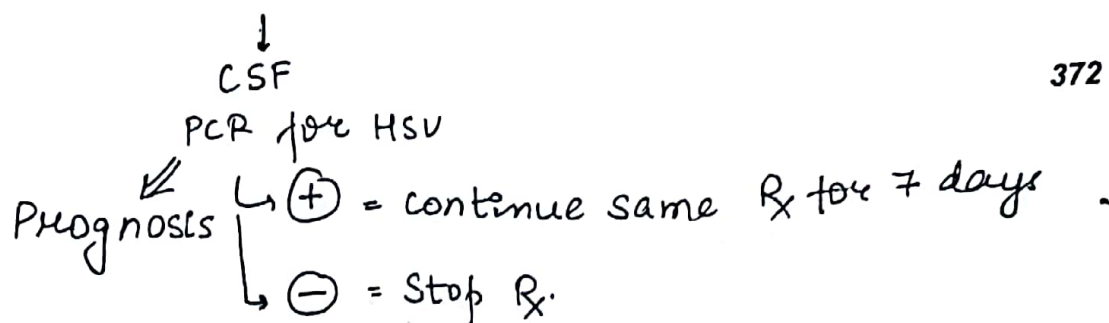
MOST SENSITIVE TEST = PCR FOR HSV IN CSF

MRI Bitemporal Hyperintensities.

	T_1	T_2 ↑ =itis
Brain	↑	↓
CSF	↓	↑

Rx Acyclovir - 10mg/kg IV 8hrly x 14 days





PROGRESSIVE MULTIFOCAL LEUCOENCEPHALOPATHY (PML)

Jc Virus → oligodendrocytes
Inclusion bodies

A/C -

Immunocompromised host
↳ HIV + (80%, M/C host)
Transplant Recipient

C/F - Visual field Defects. (M/C)

Inv

MRI → Hyperintensities
→ Demyelination

↓
CSF (PCR for Jc virus)

↓
Brain Biopsy

Rx not available

Prognosis Death 3-6 months of onset

PRION DISEASE

373

CREUTZFELD JACKOB DISEASE (CJD)

DNA/ RNA (-)

Transmittable $\begin{cases} \rightarrow \text{Dural Grafts} \\ \rightarrow \text{Corneal Grafts} \end{cases}$

C/F -

Dementia + myoclonus (M/G)

Inv

EEG - Biphasic waves

Brain Biopsy - spongiform degeneration

R_x - not available

NCC [Neurocysticercosis]

Agent = *Taenia solium*

Agent = Tactical Security

HOST = $\begin{cases} \text{DEFINITIVE} = \text{Human} \\ \text{INTERMEDIATE} = \text{PIG} \end{cases}$

accidental intermediate Host

via \rightarrow consumption of undercooked Pork \downarrow
 \rightarrow consumption of undercooked raw vegetables

C/F- seizure (M/c)

gmv -

CE \rightarrow CT
CE \rightarrow MRI

scaler \otimes Ring enhancing Lescons

STAGES

374

(viable) VESICULAR	Oedema +
(Dying) COLLOIDAL	+++
(Dead) CALCIFIED	-

Rx

ANTI - PARASITIC

[DOC]

→ ALBENDAZOLE

PRAZIQUENTAL

↓
15 mg/kg / Day x 8-28 days

+ Steroids

+

A.E.D. x 6 months

↓
CT Scan

↓
Calcified

Taper 2-3 months

↓
STOP

↓ OTHER TYPES OF CUS

[AIDP]

<4wk

Motor

Sensory

>90% children
mostly

GM, Ab +ve

[AMAN]

motor

only

children

young adult

GD, Ab

[AMSAN]

M=S

Mostly
adult

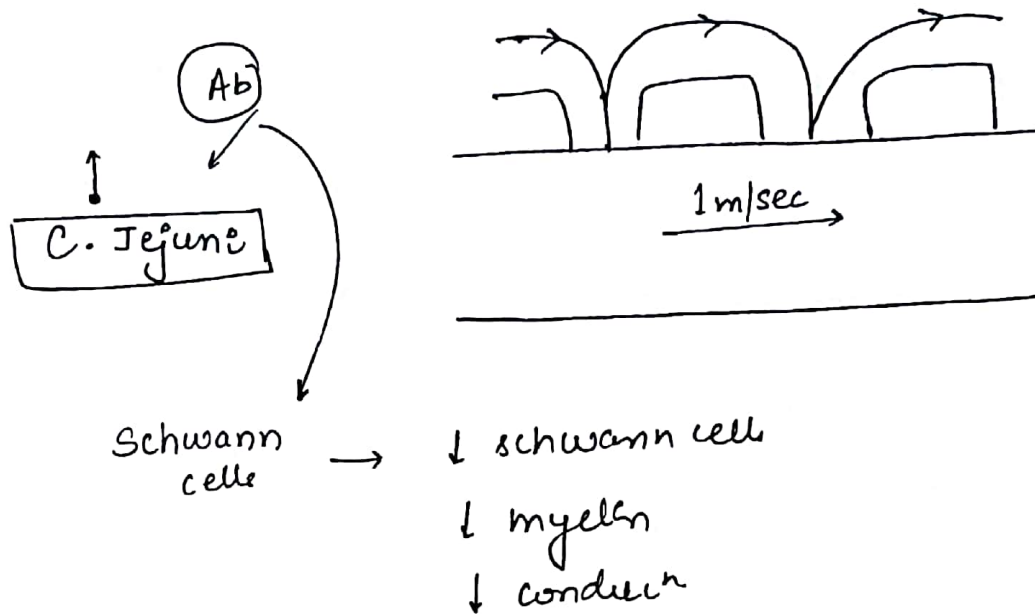
Worst Prog.

[CIDP]

>9wk.

GUILLIAN BARRE SYNDROME

375



- Post Infectious
- Demyelinating
- Poly neuropathy

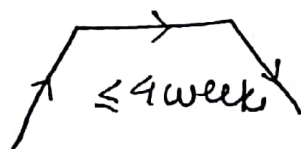
VACCINES causing GBS :-

- RABIES (neural)
- Influenza

C/F

ASHBURY CRITERIA

→ Ascending Paralysis → Symmetrical
 Distal → Proximal → ≤ 4 weeks



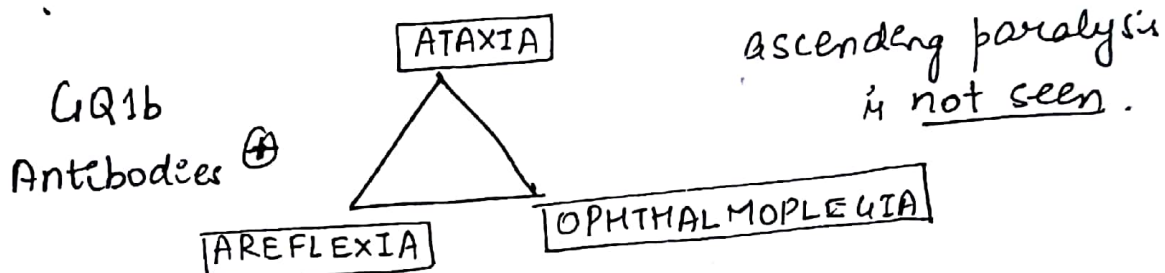
Areflexia
Minor sensory
Bladder - spared

M/c cranial N/V Invol³⁷⁸
= VIIth (B/I, LMN)

ACUTE INFLAMMATORY DEMYELINATING POLYNEURO
PATHY
(AIDP)

VARIANT OF GBS

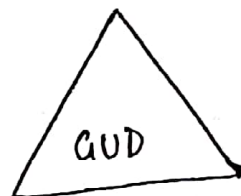
MILLER FISCHER VARIANT / SYNDROME



MILLER FISCHER TEST \checkmark (DNB)

Done In Normal Pressure Hydrocephalus

CSF Drained (30ml)



↓
Cognition

↓
Improved

then go for
V-P-Shunting

Inv For GBS

- 1) Nerve Conducⁿ Study
 - ↓ N/V conducⁿ velocity
 - ↓ A.P.

2) CSF

377

↑ Albumin
No pleomorphism } Albumino cytological
Dissociation.

Rx

- 1) IVIg ~~2mg~~ 2gm/kg over 5 Days. } Both are equally effective
- 2) Plasmapheresis } Best in 1st 14 Days

Steroids is not recommended

PROGNOSIS

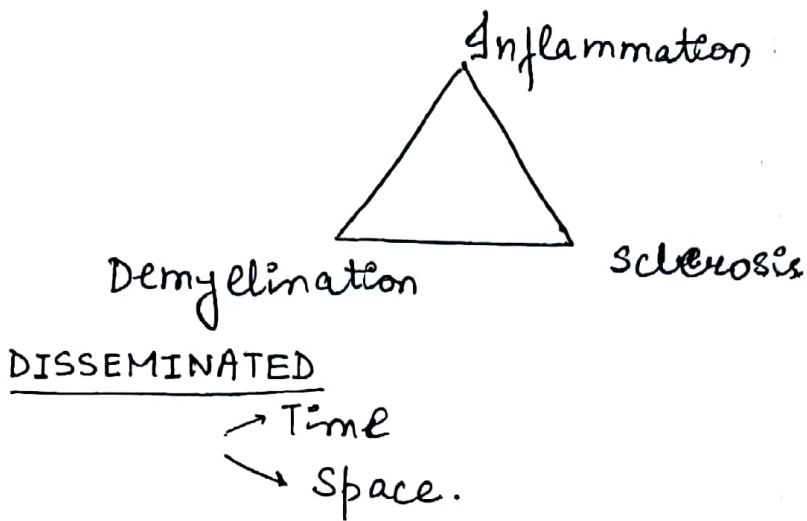
Recovery occurs in 85% [IVIg + Plasmapheresis will not alter the sequelae]
Sequelae → 10%
Death → 5%

INFLAMMATORY MYOPATHY

	DERMATO MYOSITIS	POLY MYOSITIS	INCLUSION BODY MYOSITIS
AGE	Any	>20yrs	>50yrs
MUSCLE INVOL.	Proximal	Proximal	Distal
SKIN Changes	+	-	-
Assoc malignancy	+ (15%)	-	-
EYE	(N) (Creat. Kinase ↑↑)	(N) ↑↑	(N) ↑↑

MULTIPLE SCLEROSIS

378



C/F

1) SENSORY

1st M/C symptom

↑ exposure to HEAT ⇒ UTHOFF SIGN

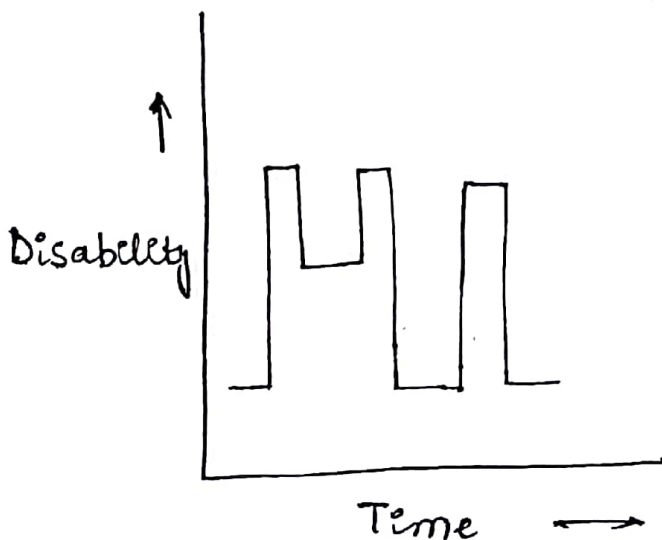
ICE PACK TEST

Cold ⊖ Ache ⇒ In M/C pts.
Weakness ↓

② OPTIC NEURITIS

③ SPASTICITY

TYPES



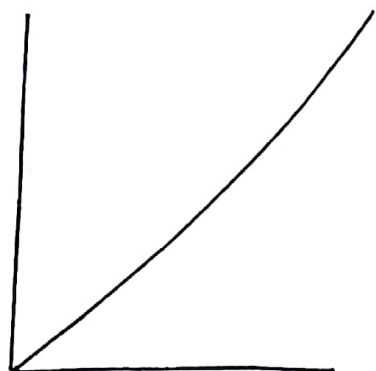
RELAPSING

~~REMITT~~

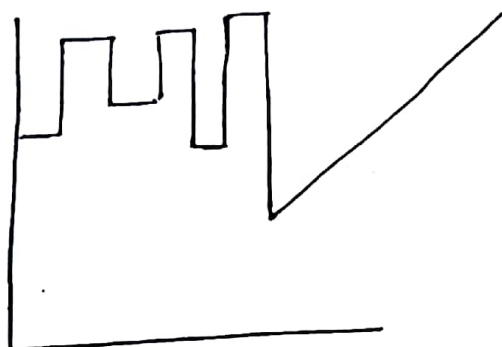
REMITTING

[RRMS]

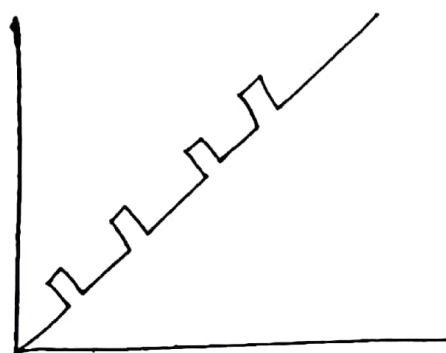
85%



1° PROGRESSIVE
MS (PPMS) 15%



2° PROGRESSIVE
MS (SPMS)



PROGRESSIVE RELAPSING
MS (PRMS)

STAGING

MS = EXTENDED DISABILITY SCORING SCALE (EDSS)

SAH = HUNT & HESS SCALE

MG = OSSERMAN GRADING

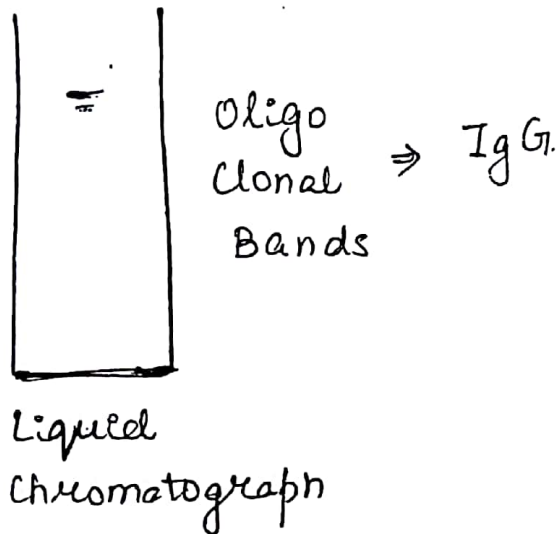
INV

380

MAC DONALD CRITERIA

MRI → Demyelination
 ↓
 Plaque } Periventricular

CSF

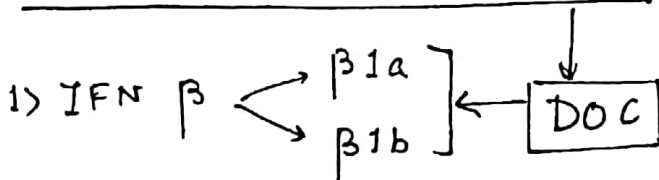


R_x

ACUTE ATTACK

METHYL PREDNISOLONE (DOC)

DISEASE MODIFYING AGENTS



2) Glatiramer

3) Fingolimod [ORAL]

4) Natalizumab [BEST] → S/E = PMLE

D/D of DESCENDING PARALYSIS

381

Botulism

Polio, Porphyria

Diphtheria

ENDOCRINE

- Dr. Achin

PROLACTIN

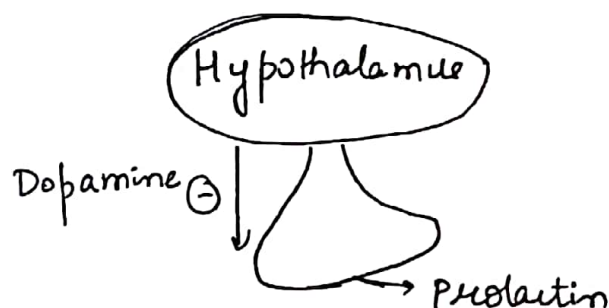
Secreted in Ant Pituitary

Prolactin making cells LACTOTROPH

FUNC:-

1> Induce & maintain the process of lactation

2> prolactin hormone $\xrightarrow{\ominus}$ GnRH \rightarrow LH \downarrow
 \downarrow \rightarrow \downarrow ovulation
 sexual drive \leftarrow \downarrow Testosterone \rightarrow \ominus menstruation
 \downarrow
 Spermatogenesis



HYPERPROLACTINEMIA

ETIOLOGY -

A) PHYSIOLOGICAL

1> Lactation

2> ♀

\uparrow Estrogen $\xrightarrow{+}$ \uparrow PL

3> Sleep [NREM sleep]

4> Chest wall stimulation

\rightarrow nipple stimulation

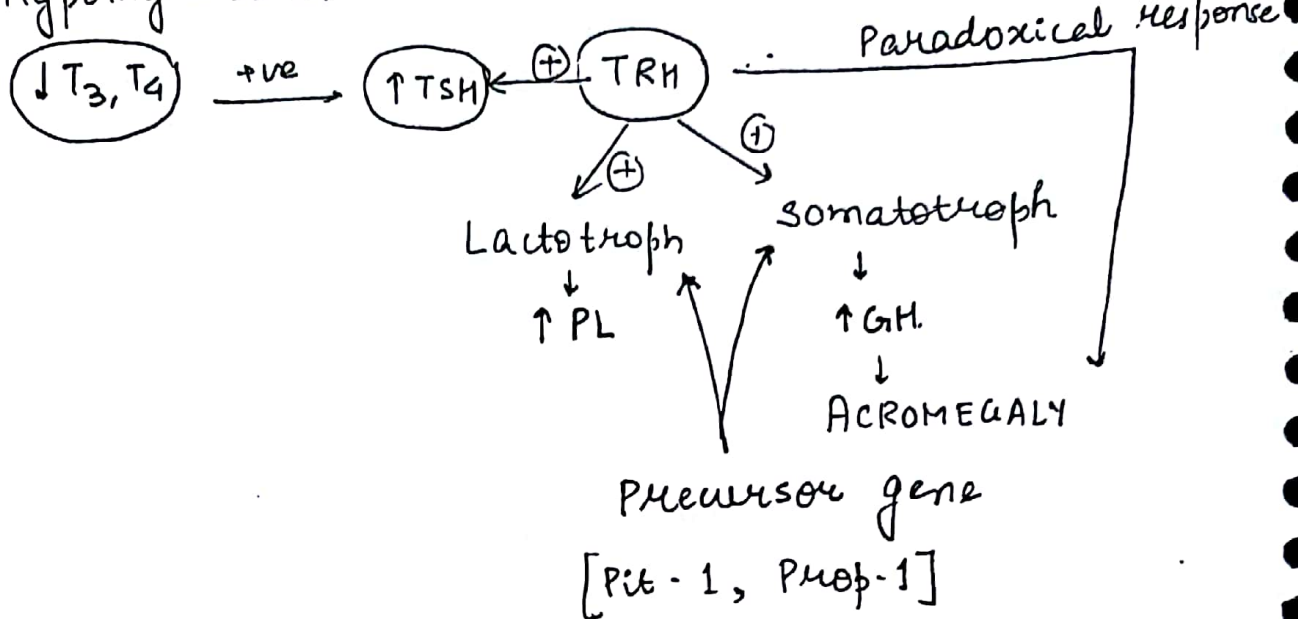
\rightarrow chest trauma or surgery

→ herpetic lesions

386

5.8) SYSTEMIC DISORDERS

1) Hypothyroidism



2) CKD

→ ↓ excretion of prolactin



3) SEIZURE

Post Ictal (30 mins)

C) DRUGS (Iatrogenic)

Dopamine \ominus

→ Typical Antipsychotics

└ Haloperidol
└ CPZ

→ Atypical Antipsychotics

└ Risperidone

→ Metoclopramide

Dopamine Depletors

CH₃ Dopa

Reserpine

CCB - verapamil

H₂ ANTAGONIST

Ranitidine

Cimetidine

⇒ These drugs cause hyperprolactinemia due to blockage of Infundibular Pathway

D> PITUITARY ADENOMA

PROLACTINOMA → M/c type

<10mm

MICRO (90%)

F:M = 20:1

>10mm

MACRO (10%)

F:M = 1:1.

C/F → ♀ → Galactorrhea - 80%
↳ B/L.

Amenorrhoea

↑ PL → ↓ LH

↓ ovulation

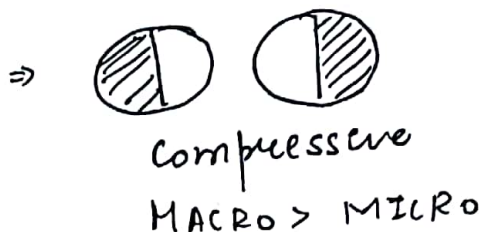
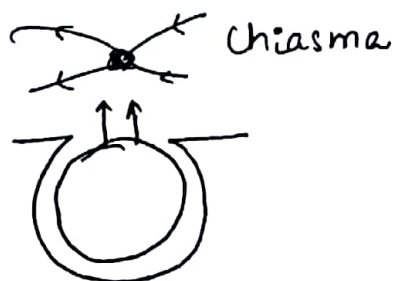
↓ Estrogen

↓ Osteoporosis

Infertility (M/c presentation)

♂ → ↓ Libido
Azoospermia
Infertility

388



S. PROLACTIN

(N) = 5 - 25 $\mu\text{gm/L}$

- ↳ PHYSIOLOGICAL → 25 - 40
- ↳ IATROGENIC → 25 - 100
- ↳ PRACTINOMA → > 200
- ↳ MACRO PROLACTINOMA - > 250

Stop offending drug

Reassess PL after 72 hours

MACROPROLACTIN

Symptoms (-)

Prolactinoma (-)

S. Prolactin ↑↑↑
[FALSE HIGH]

PROLACTIN = Peptide hormone
(198 A.A)

↳ 85% monomeric

HOOK EFFECT

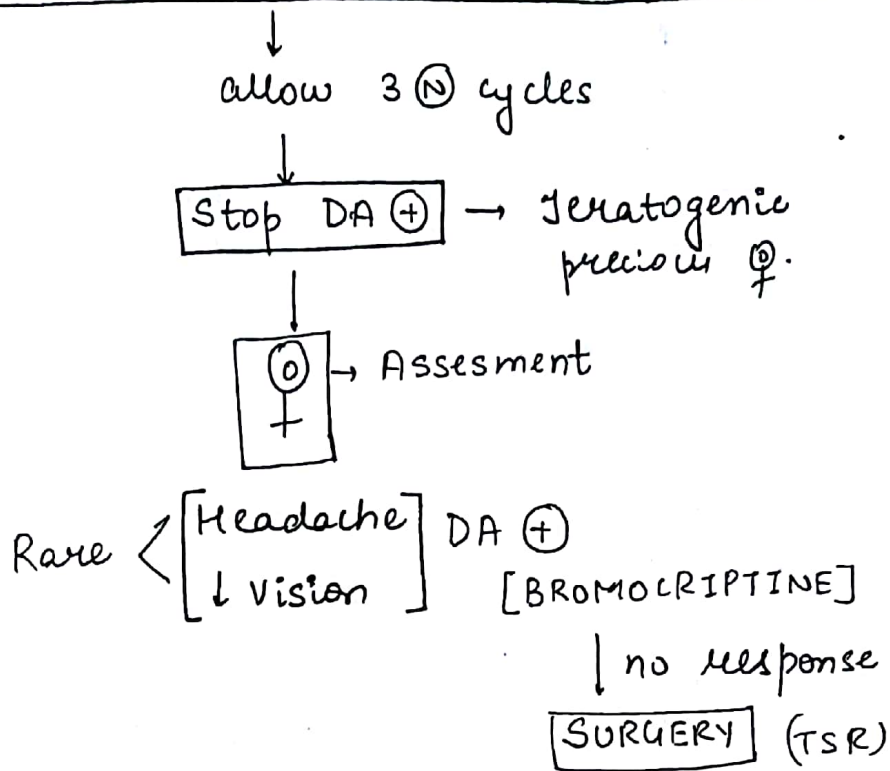
Symptoms (+)

Prolactinoma (+)

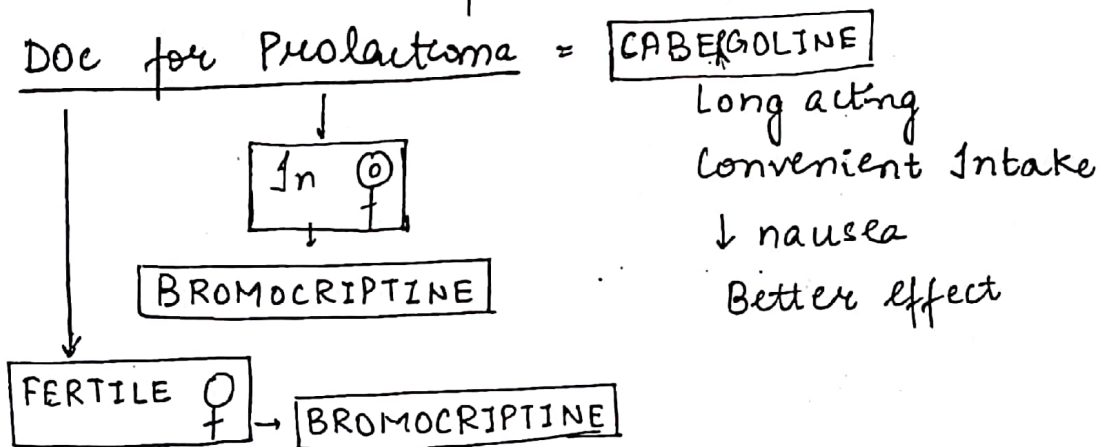
S. Prolactin (N)
[FALSE (N)]

PROLACTINOMA ON DA (+) WANTS TO CONCEIVE

390



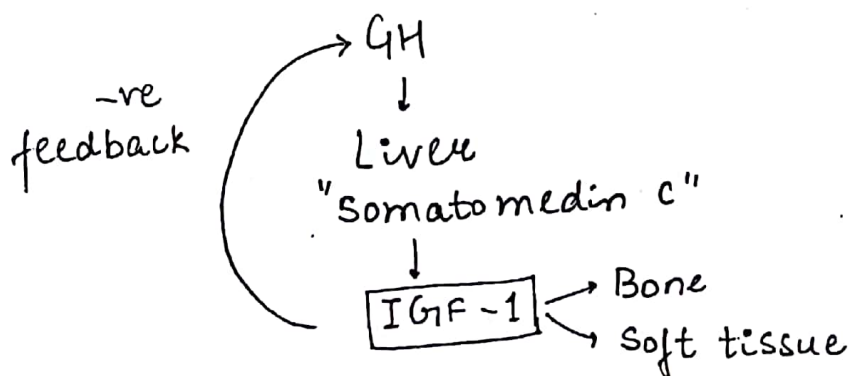
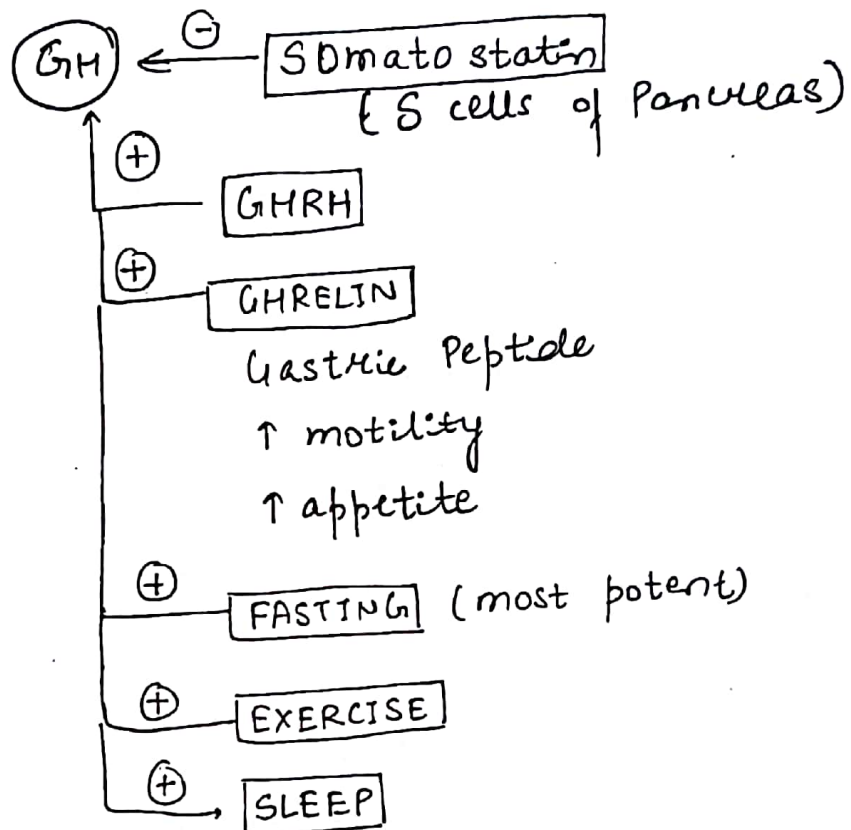
Prolactinoma is ⊙ are asymptomatic



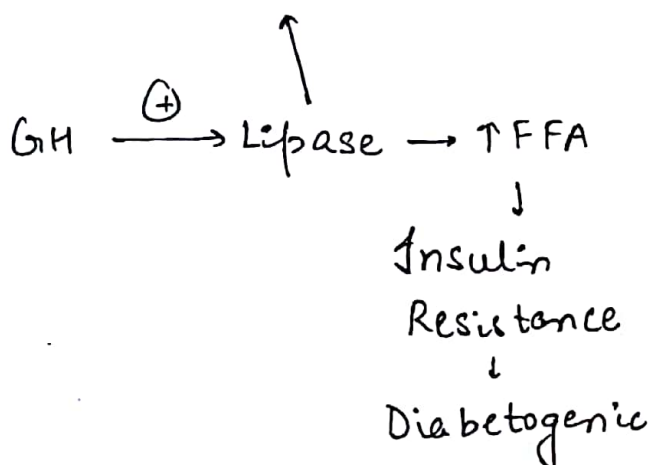
GROWTH HORMONE

391

- Released from Ant. Pituitary
- By SOMATOTROPHS (Most abundant cells) 50%)
 - > Lactotrophs > Gonadotrophs
 - (20-30%) (10-20%)



GH	IGF-1
CARBOHYDRATE	
Diabetogenic	Anti diabetic
PROTEIN	
ANABOLIC	ANABOLIC
FAT	
LIPOLYTIC	ANTILIPOLYTIC



$\uparrow GH$

↳ epiphyseal fusion.

↳ BEFORE = GIGANTISM

↳ AFTER = ACROMEGALY

ACROMEGALY

ETIOLOGY

$\uparrow GH$

PITUITARY

↳ Somatotrophic
Adenoma (M/cc)

Loss of feedback

↳ HAMMO SOMATOTROPHIC

ADENOMA $\rightarrow \uparrow PL$

$\uparrow GH$

$\uparrow GHRH$

HYPOTHALAMUS

HAMARTOMA

ECTOPIC

BRONCHIAL CARCINOMA

ECTOPIC

ISLET CELL CA of PANCREAS

393

C/F

CVS → LVH
Diastolic Dysfuncⁿ
HTN
CAD

M/CC of DEATH
ACUTE M.I.

Resp → Nasal turbinate Hypertrophy
Obstructive sleep apnoea (OSA)

GIT → ↑ Liver + spleen (Hepatosplenomegaly)

Q Colonic Polyps >> Cancer
↓
Benign

ENDOCRINE → DM (Insulin resistance)
Goitre

SKELETAL → Tall Stature
Large Digits
Prognathism
Jaw malocclusion
[↑ space betⁿ lower incisors]
Fleshy nose.

INVESTIGATION

394

1> GH ASSAY → not useful test



2> IGF-1 ASSAY
Best screening Test

3> GH SUPPRESSION TEST → confirmatory Test

$$[GH \propto \frac{1}{\text{glucose}}]$$

75 gm glucose (oral)



R_x
TSR - R_{OC} → F/B → ADJUVANT THERAPY

[Initial therapy]

Somatostatin
octreotide
Cancerostide

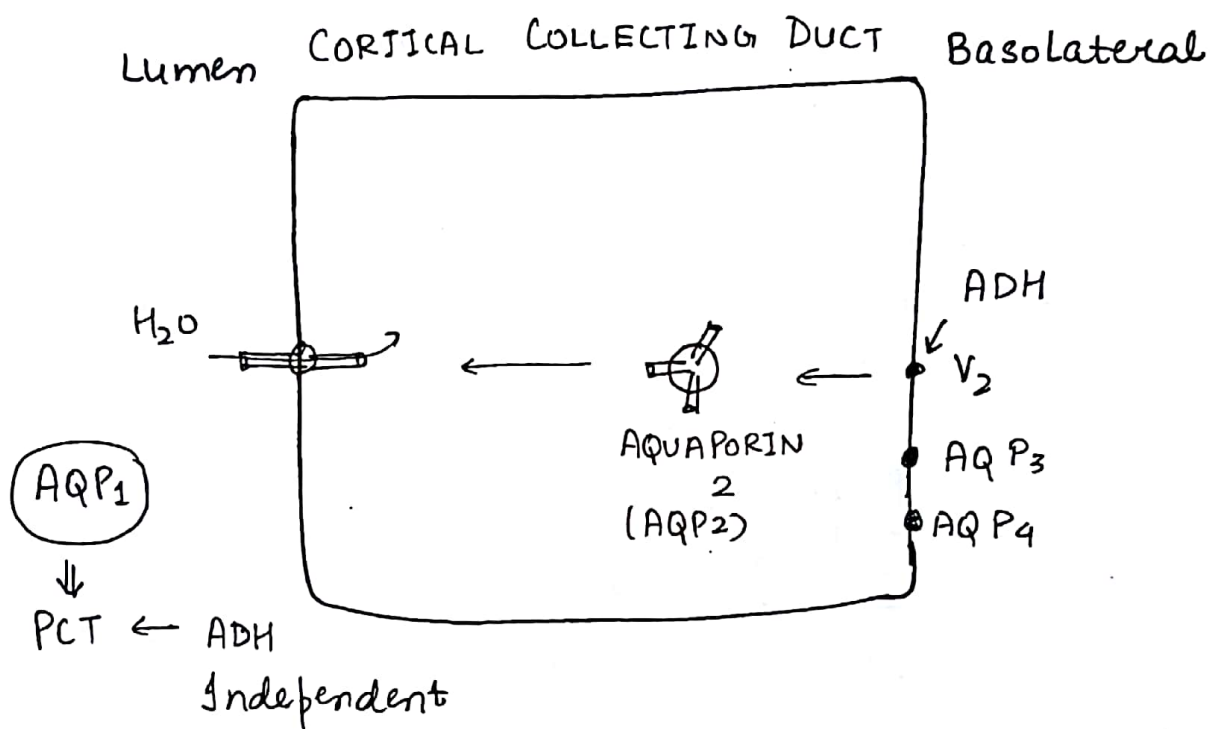
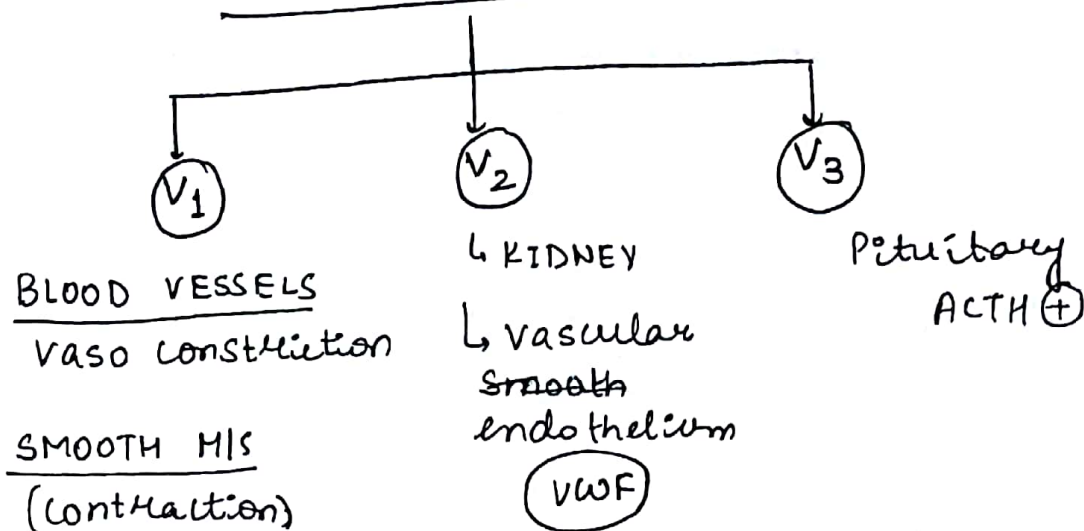
GH ⊖
Pegvisomant

INSULIN STIMULATION TEST

GH $\propto \frac{1}{\text{glucose}}$ → on giving Insulin.
glucose ↓ → GH ↑ (N)

Dwarfism → GH unchanged

ADH / VASOPRESSIN



(N) values

S. Osmolality = 275 - 295 mosm/L

Urine osmolality = 300 - 1000 mosm/L

Sr. Na⁺

135 - 145 meq/L

Sr. K⁺

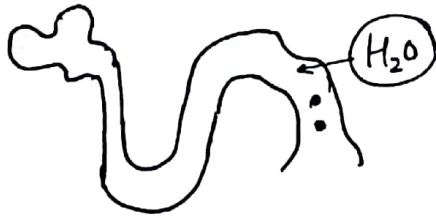
3.5 - 5 meq/L

POLYURIA

396

$> 50 \text{ ml/kg/day}$

$> 3 \text{ L/day}$



$\uparrow \text{ solute} = \downarrow \text{H}_2\text{O}$

Isosmolar

SOLUTE/OSMOTIC DIURESIS

Glucose

Mannitol

Ca^{2+}

\downarrow
Urine osmolality

> 300

(N)

DILUTE

$\text{H}_2\text{O} > \text{Solute}$

Urine osm < 300

→ DI

→ Psychogenic Polydypsia (PP)

H_2O Deprivation Test

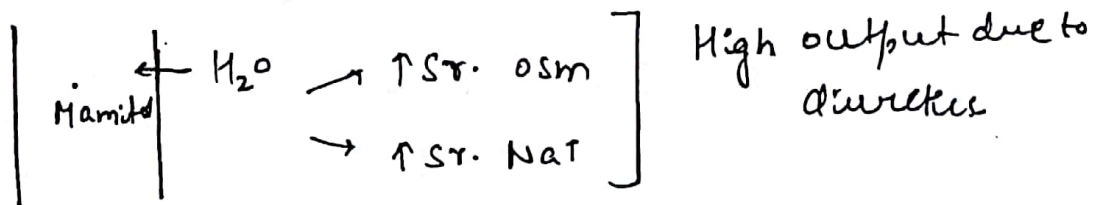
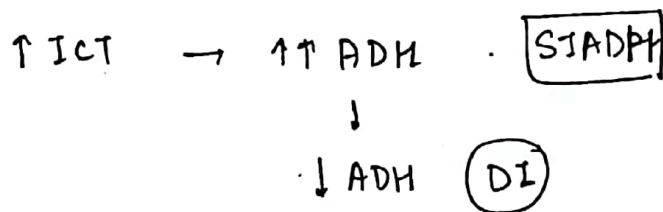
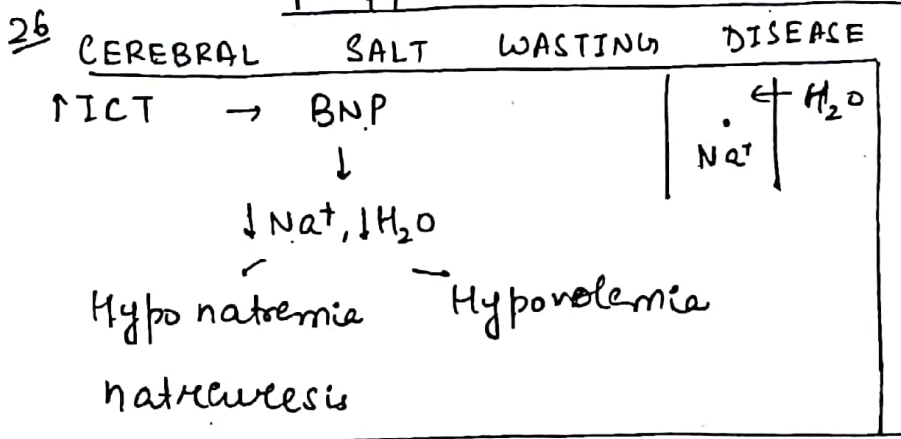
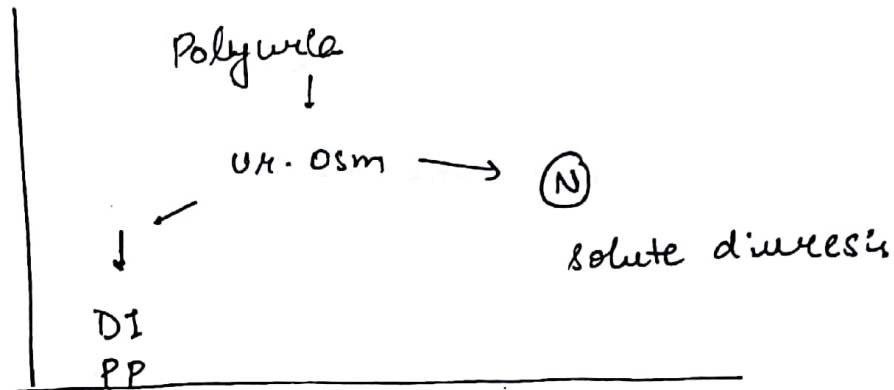
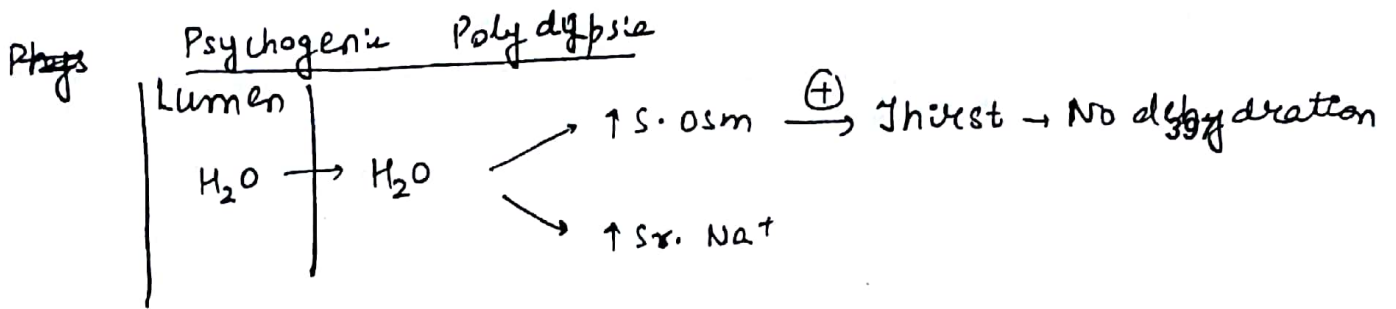
Urine osm. $\rightarrow \uparrow = \text{P.P.}$

\hookrightarrow unchanged = D.I.

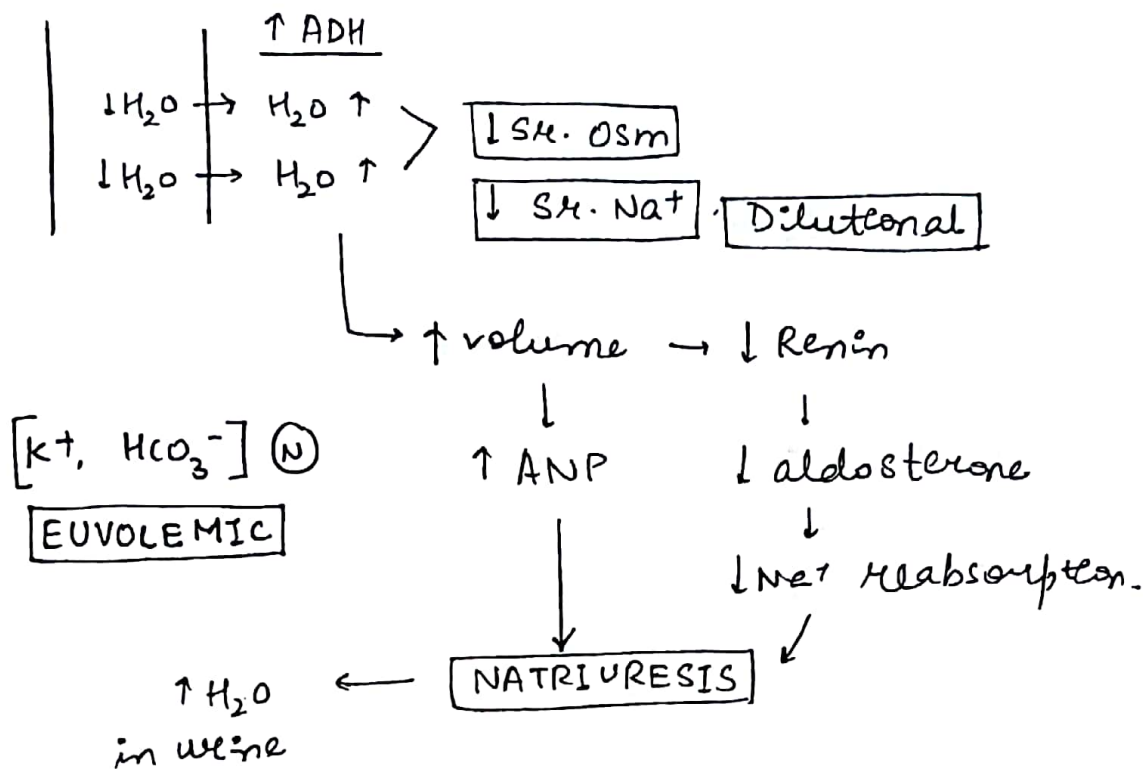
ADH Stimulation Test

Urine osm $\rightarrow \uparrow = \text{ADH Def.}^n$

\hookrightarrow unchanged = ADH Resistance
nephrogenic DI



SIADH [Syndrome of Inappropriate ADH] 398



HYPONATREMIA

HYPOVOLEMIC
Cerebral Salt
Wasting Disease

EUVOLEMIC
SIADH
 \downarrow
H₂O Loading Test

Pt. produce less
urine than (N) pt

R_x = H₂O Restriction R_{oc}

ADH \ominus \rightarrow DEMECLOCYCLINE
 \rightarrow VAPTAN (Doc)

HYPERVOLEMIC
CCF
CKD
Chr Liver Disease

$\boxed{\text{Na}^+}$

399

$\boxed{[N]} = 135 - 145 \text{ meq/L}$

$>120 = \text{Asymptomatic}$

$\boxed{110-120} = \text{GI symptoms}$
↳ nausea

$\boxed{100-110} = \text{mild CNS symptoms}$
giddiness
Ataxia

Seizures $\rightarrow \boxed{<100}$ cerebral oedema

PARATHYROID HORMONE

$\downarrow \text{Ca}^{2+} \rightarrow \uparrow \text{PTH}$

↳ Bone = Resorption

↳ Intestine = Absorption

↳ Kidney = Reabsorption

$\boxed{\uparrow \text{PTH}}$

4 $\boxed{2^\circ} \rightarrow \text{CKD}$
Vit D deficiency
Malabsorption.

$\boxed{1^\circ} \rightarrow \text{Parathyroid} \rightarrow \text{Hyperplasia}$
 $\boxed{\text{Adenoma}} [\text{M/c/c}]$
↓
M/c type = solitary
M/c site = Inf. Pth lobule.

3° = PTH hyperplasia → ADENOMA (3°)

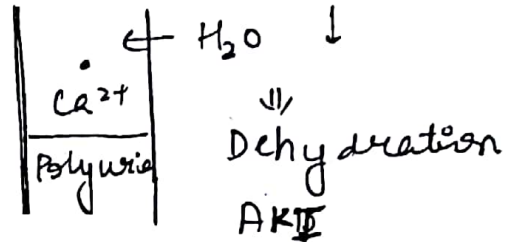
400

2° 1°

HYPERCALCEMIA

C/F -

- nausea, vomiting
- Constipation
- Bony pains ⊕
- Renal calculi
- Abdominal Pain
- depression
- Psychosis



Rx -

- 1) Hydration.
- 2) Diuretics
 Calcium → Loop Diuretics
- 3) Bisphosphonates
 ⊖ osteoclastic activity
 DRONATES.
 [Delayed onset of Action]
- 4) GALLIUM }
5) PLICAMYCIN } → Osteoclast ⊖
- 6) CALCITONIN
- 7) DIALYSIS

PSEUDO HYPO PTH

401

\downarrow Sx. Ca^{2+}

Sx. PTH \uparrow

PTH resistance

ALBRIGHT HEREDITARY OSTEODYSTROPHY (AHO)

Short stature

~~Round~~ Round Face

Short 4th/5th metacarpal. (Brachydactyl)

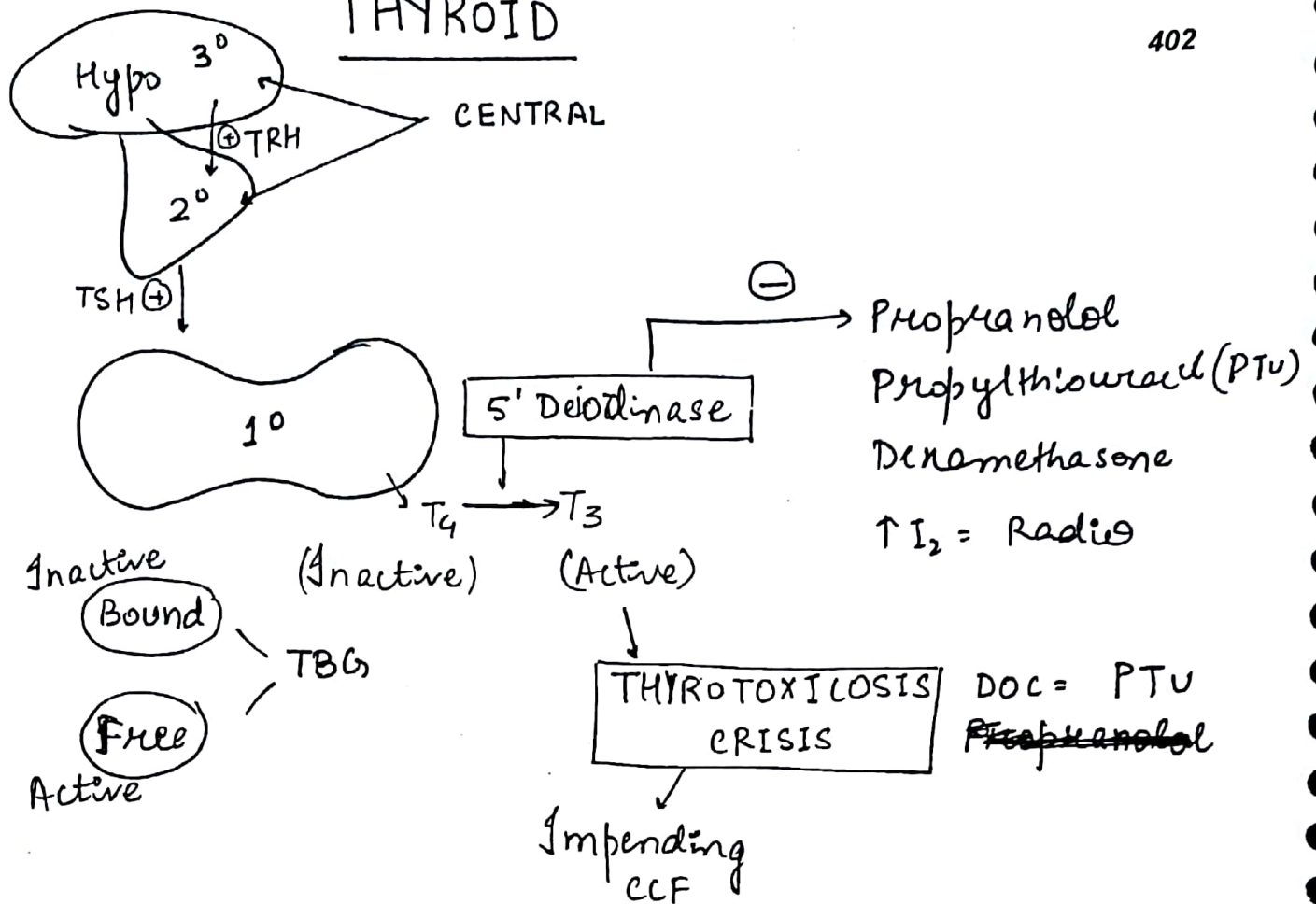
PSEUDO PSEUDO HYPO PTH

Sx. Ca^{2+} = (N)

Sx. PTH = (N)

AHO phenotype (+)

THYROID



	TSH	FT ₃	FT ₄
HYPOTHYR (1°)	\uparrow	\downarrow	\downarrow
HYPERTHYR	\downarrow	\uparrow	\uparrow
2° HYPOTHYR	\downarrow	\downarrow	\downarrow
SUBCLINICAL HYPOTHYR	\uparrow	Low (N)	Low (N)

HYPOTHYROID

Weight Gain

Fatigue

Cold Intolerance

Constipation

Menorrhagia

M/C Amenorrhoea

↓ H.R.

mild Diastolic HTN

Delayed Relaxation of
Jerk

[HUNG UP REFLEX]

R_x

HYPOTHYROIDISM

L-Thyroxine
[1.6 mg/kg/day]

↓ DOSE = elderly
IHD

↓
TSH after [6 weeks]

[N] = 0.35 - 5

[Target = 0.35 - 2.5]

→ L-Thyroxine x Lifelong

TSH

10

↓

8

L-Thyroxine

75 µg/day

↓ +25

100 µg/day

HYPERTHYROID

403

Weight Loss

Anxiety

Heat Intolerance

Diarrhoea

Amenorrhoea

↑ H.R.

↑ S.B.P. / ↑ D.B.P.

Fine Tremors

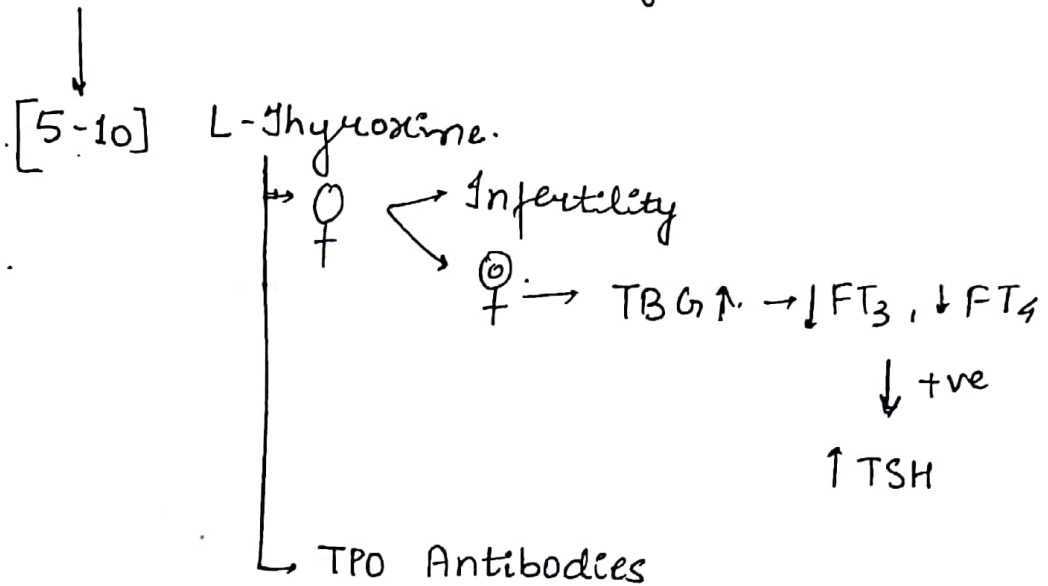
Exophthalmos

SUBCLINICAL HYPOTHYROID
 \uparrow TSH, $[FT_3, FT_4]$ low (N)

404

Rx-

TSH $>10 \Rightarrow$ start L-thyre



ADRENALS

405

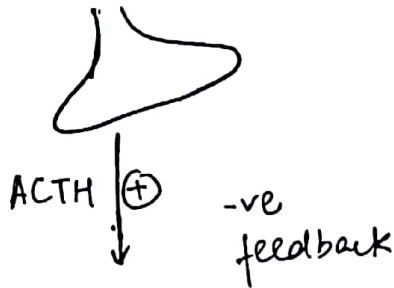
CUSHING SYNDROME

Loss of -ve feedback

ETIOLOGY

A) EXOGENEOUS / IATROGENIC [M/C]

B) ENDOGENEOUS



ACTH

DEPENDENT (90%)

INDEPENDENT (10%)

Pituitary 75%

Adenoma [F:M=4:1]

M/C endogenous cause

→ ECTOPIC ACTH 15%

[F:M=1:1]

M/C malignancy → small cell Ca of lung

• medullary Ca of thyroid

• Pheochromocytoma

• CARCINOMAS → Bronchial
→ Thymus
→ Pancreatic

ADRENAL [F:M=4:1]

Adenoma (5-9%)

CA (1%)

Hyperplasia (<1%)

M/C → CUSHING DISEASE

Cushing Syndrome due to Pituitary Adenoma.

C/F :-

406

↑ CORTISOL → ↑ Gluconeogenesis

1) PROTEIN → MYOPATHY (proximal)

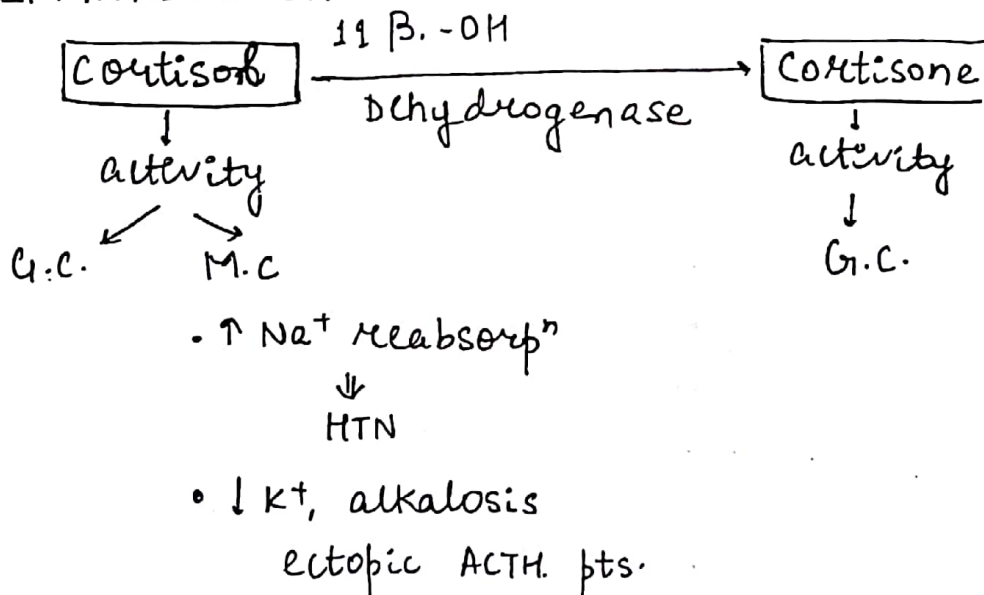
↳ s/c Tissue Tear = STRIAE Purplish colour due to rupture of vessels.
↳ THIN SKIN
↳ EASY BRUISING.

2) FAT Redistribution of fat
CENTRIPETAL OBESITY

↳ BUFFALO HUMP
↳ MOON LIKE FACE

3) DM

4) HYPERNATREMIA



5) ♀
Oligomenorrhoea → Amenorrhoea
Hirsutism

6> CNS -

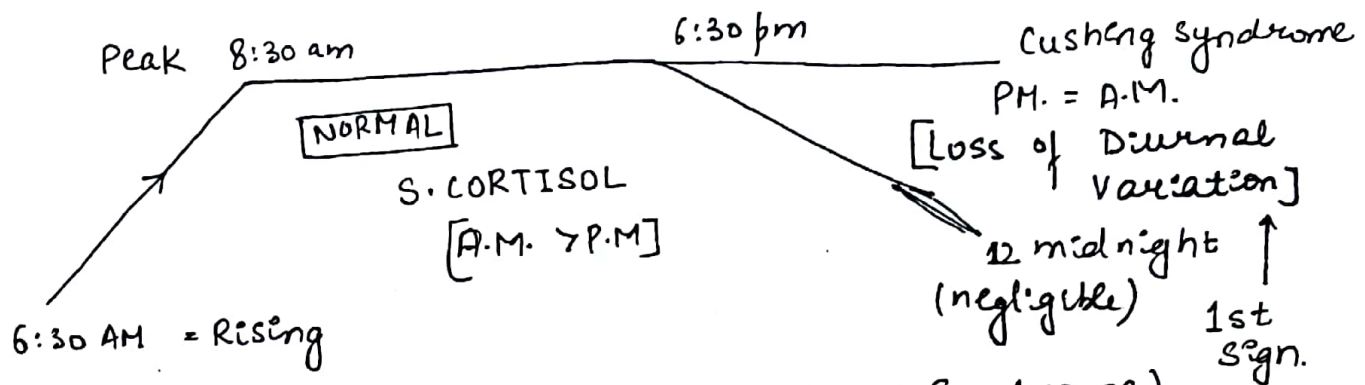
↑ appetite

↓ sleep

Euphoria

[Psychosis]

407



PSEUDO-CUSHING (mimic Cushing Syndrome)

Chronic ~~alcohol~~ alcoholics

Psychotic pts.

Pts = Hyperthyroidism

Pt = Depression.

CLINICAL SUSPICION OF C.S.

WEIGHT GAIN (80%) = Thin skin > HTN (80%) (75%)

1st M/C symptom

> central obesity (50%)

> ↓ K⁺, alkalosis (15%)



SCREENING TEST

~~SRI~~ SCREENING TEST

408

- 24 HR. URINARY CORTISOL ↑↑
- MIDNIGHT S. CORTISOL ↑
- ORAL DEXA CHALLENGE TEST [BEST]

1mg DEXAMETHASONE @ 11:00PM

(oral) ↓

S. CORTISOL @ 9:00AM

↳ (N) = (N)

↳ C.S. = ↑ (due to loss of -ve feedback)

CONFIRMATORY

(4mg) 0.5mg DEXA i/v 6hrly x 2 days

↓
S.H. cortisol → (N) = C.S. ⊖ ⊖

↳ ↑ . C.S. ⊕ ⊕

[LOW DOSE DEXA TEST]

ETIOLOGY H/O - exogenous

ACTH

↑
DEPENDENT

↳ PITUITARY ADENOMA
↳ ECTOPIC ACTH.

↓/ (N)
INDEPENDENT

ADRENAL ADENOMA
[CT Abdomen]

MRI can't visualize pituitary adenoma (2-5mm)

1) INF- PETROSAL SINUS SAMPLING (IPSS)

(CRH)

↓ ⊕

ACTH

↓
Sample

Petrosal sinus (PS)

Peripheral vein (PV)

RATIO

409

$\frac{PS}{PV} \uparrow \Rightarrow$ Increased
 $PV \downarrow$

PITUITARY ADENOMA

$\frac{PS}{PV} \downarrow =$ Decreased.
 $PV \uparrow$

ECTOPIC ACTH

2mg DEXA IV. 6hrly x 2Days

\downarrow
S. ~~cholesterol~~ cortisol
 \downarrow = Pituitary Adenoma
unchanged = Ectopic ACTH.

2) High Dose DEXA TEST

PITUITARY ADENOMA

ECTOPIC ACTH

C/F

ONSET \rightarrow Insidious

Acute

PROGRESSION \rightarrow Slow

Rapid

HYPERPIGMENTATION \rightarrow (+)

(+) (+) (+) (+)

IPSS

$\frac{PS}{PV}$ (+)

$\frac{PS}{PV}$ (-)

HIGH DOSE DEXA TEST +ve response

Unchanged.

Rx

Ketoconazole
Metyprone
Etomidate
Mitotane

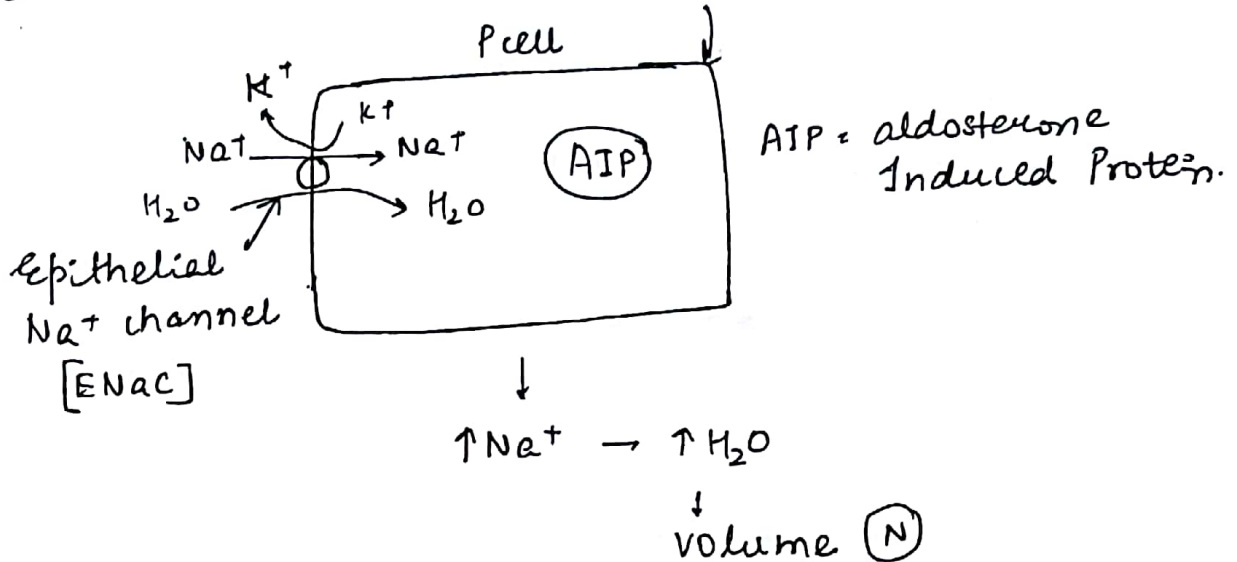
\ominus cortisol synthesis

HYPER ALDOSTERONISM

410

2°

↓ volume → ↑ Renin → ↑ Aldosterone

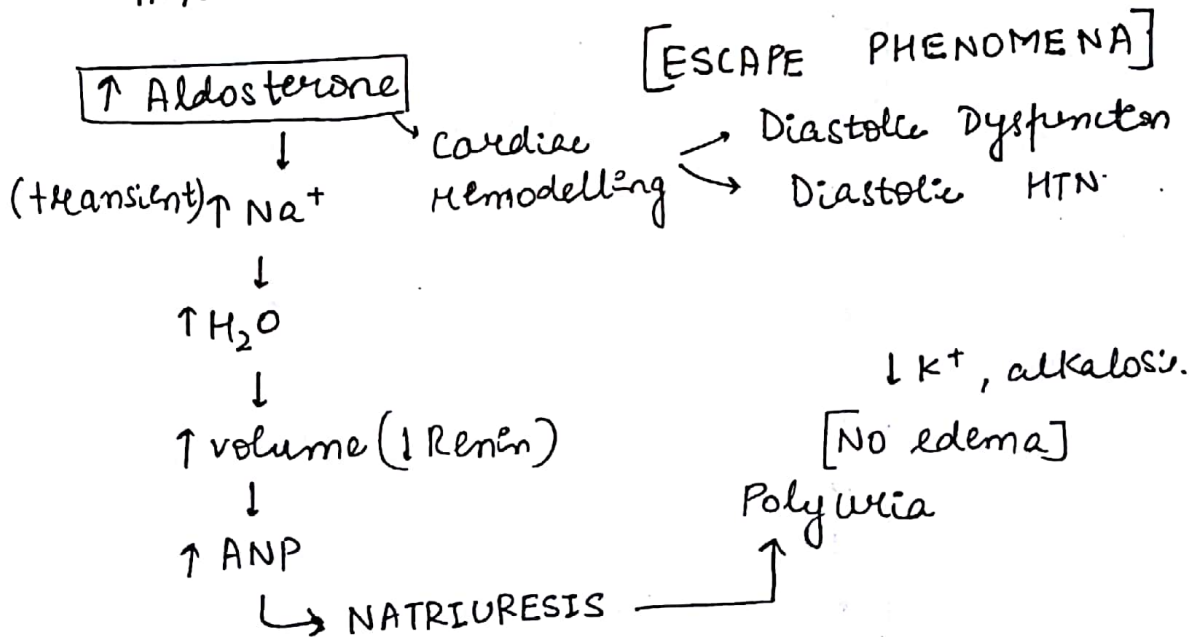


1° ← M.c.c.

1> BIL Idiopathic cortical Hyperplasia (60%)

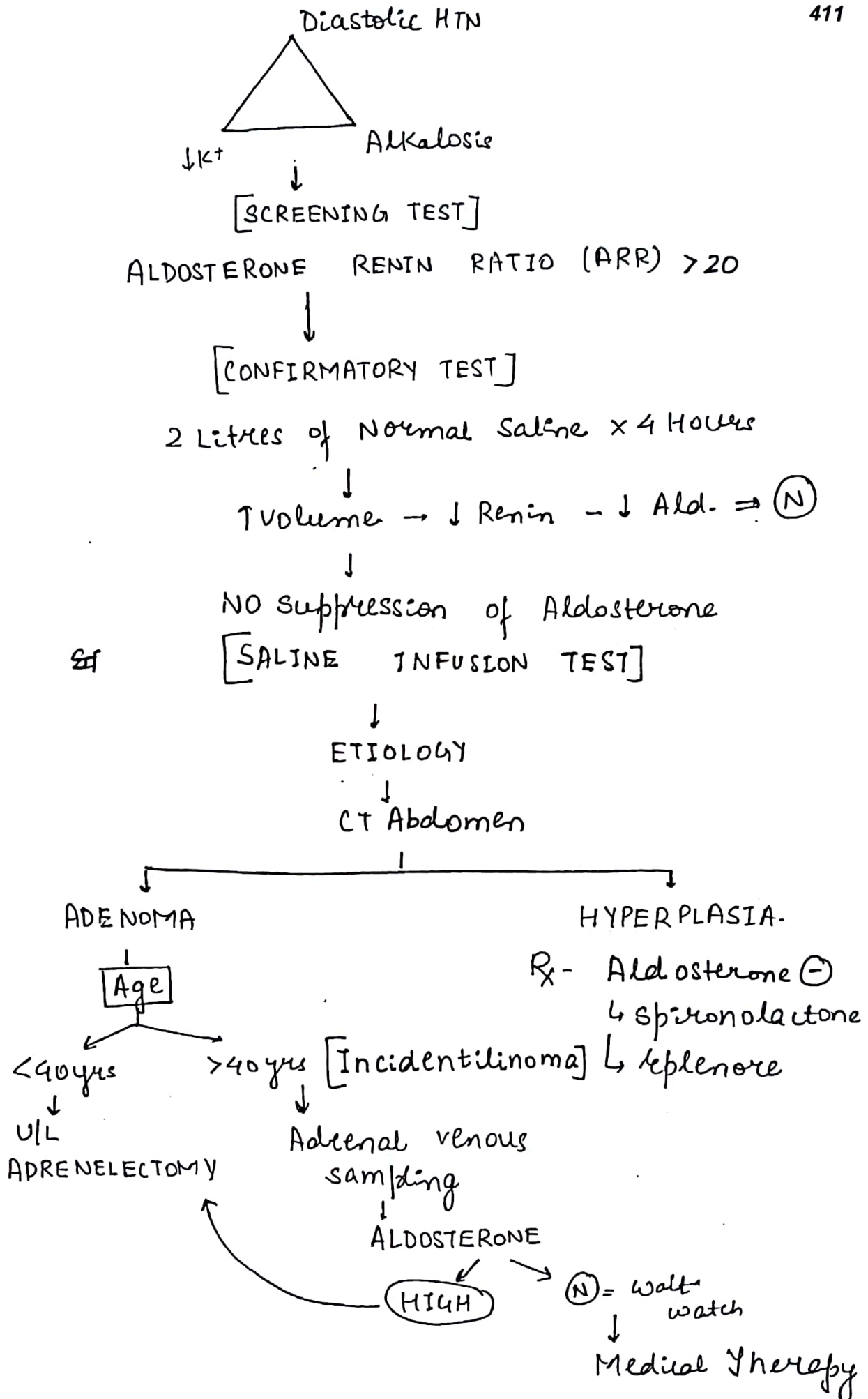
2> Adrenal Adenoma (40%)

M/c/c - CONN SYNDROME



CLINICAL SUSPICION

411



412

[SAME]



1 cortisol.

[GRA]

 $R_X -$

37

↑ Functioning of

R_x -

ADRENAL INSUFFICIENCY

413

ADDITIONAL DISEASE

1°

ADRENAL

Autoimmune (MCC in world)

TB (MCC in India)

2°

PITUITARY

- ↳ Surgery
- ↳ Trauma
- ↳ Radiation
- ↳ Apoplexy

↓ CORTISOL

DEFICIENCY

↓ G.C. ← Activity → M.C ↓

↓ GLUCOSE

↑ Protein Breakdown

wt. loss

Thin

ASTHENIA

M/C = 1st symptom

↳ Lethargy

↳ Fatigue

↓ Na⁺ ← Salt Wasting
M/C Biochemical Ab(N)

↓ ECF

↓ BP

[↑ K⁺, acidosis]

↑ ACTH

Hyperpigmentation. (localised)

↳ Oral mucosa

Conjunctive

Palmar crease

Nipple & areola region

moles, scars

ACTH administration

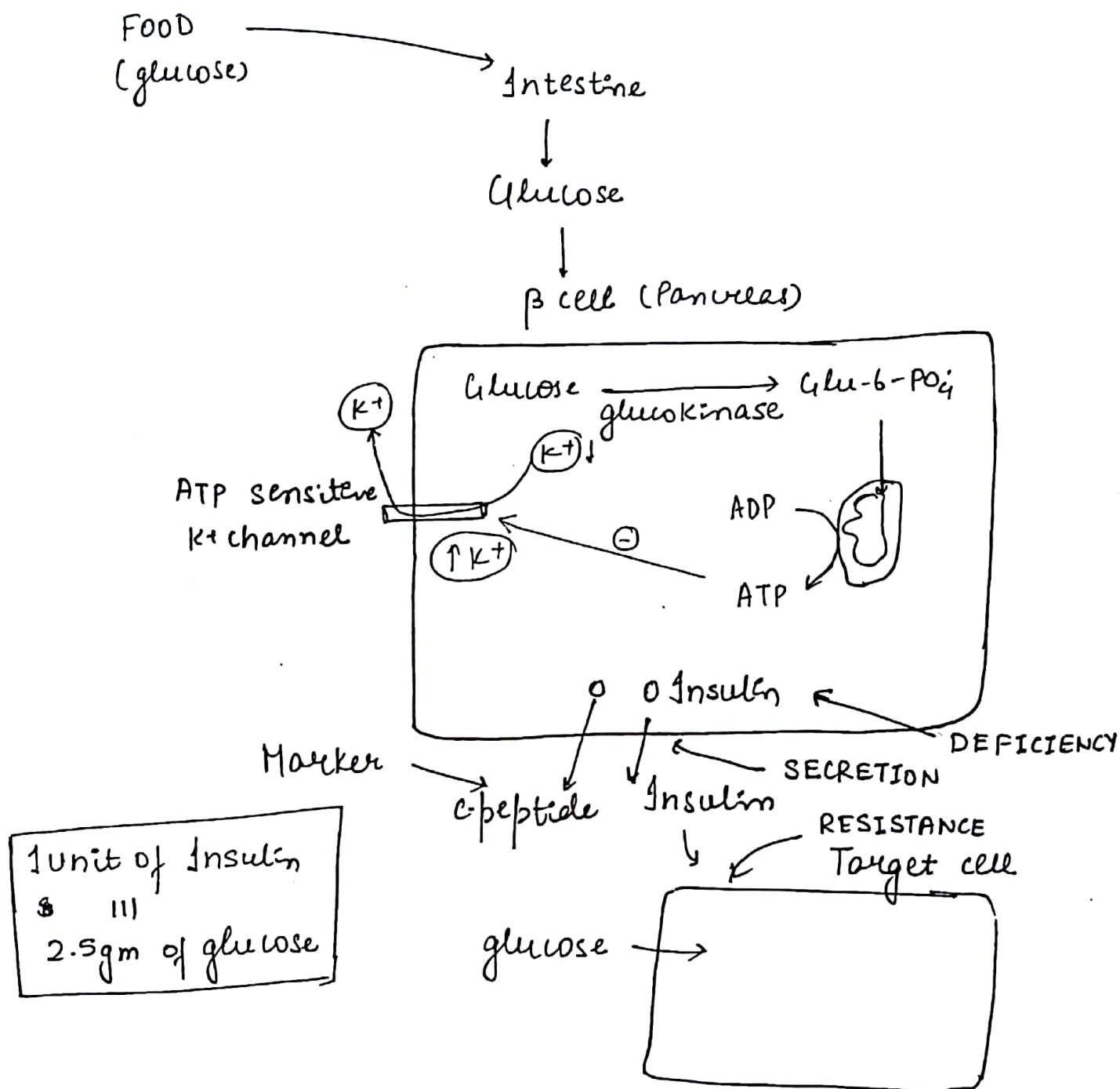
└ (N) → CORTISOL ↑

└ Addison's pt → CORTISOL (unchanged)

[ACTH STIMULATION TEST / COSYNTROPIN / SYNACTHEN
TEST]
Diagnostic Test

Rx = STEROIDS
Hydrocortisone (DOC)

DIABETES MELLITUS (DM)



Deficiency = TYPE-I

Secretion
Resistance → TYPE-II

Insulin $\uparrow \frac{1}{2} \rightarrow \downarrow$

TYPE-I

- β cell Destruction
($>90\%$)

- HLA Mediated

Aniinsulinemia

Age of onset <30 yrs

Habitus Thin

Family H/o. \oplus

HTN \ominus

Dyslipidemia \ominus

DKA

TYPE-II

Secretory Defect

Insulin Resistance

Hyperinsulinemia

>30 yrs

obese

$\oplus \oplus \oplus \oplus$

\oplus

\oplus [\uparrow TG \rightarrow \downarrow HDL]

Hyperosmolar

Non-Ketotic coma

20 yrs \longrightarrow 25 yrs
RBS $\uparrow\uparrow\uparrow$ RBS - controlled.
K.B. \oplus Insulin $\downarrow\downarrow$
Obese (OHA)
Insulin (Type 2)
(Type 1)

30 yrs \longrightarrow 35 yrs
RBS $\uparrow\uparrow\uparrow$ RBS $\uparrow\uparrow\uparrow$
Thin OHA $\uparrow\uparrow\uparrow$
K.B. \ominus Insulin
OHA (Type 2) (Type 1)

KETOSIS PRONE DIABETES
(KPD)

1.5 DM

LATENT AUTOIMMUNE
DIABETES IN ADULTS
(LADA)

MATURITY ONSET DIABETES IN ADULTS (MODY)

Onset 5-15 yrs of Age.

Thin

OHA Response

AD Inheritance

DKA \ominus

HTN \ominus

6 types of MODY

↓
TYPE 3 (M1c type)

↓
HNF-1 α Deficiency

TYPE-3 DIABETES / BRAIN DIABETES / ALZHEIMER

Insulin Resistance, Deficiency

↓
Ppt the Condⁿ

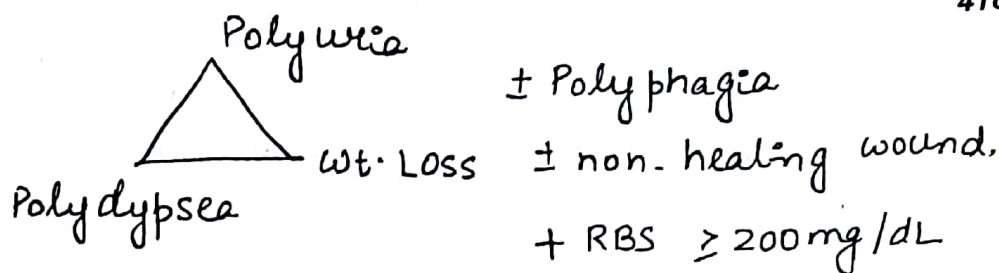
TYPE-4

Elderly >60 yrs.

OHA response (minimum dose)

DIAGNOSIS

418



or.

Fasting 8 hrs ← Fasting BS ≥ 126 mg/dL

or

Oral GTT

75 gm glucose (oral)



2 hr BS ≥ 200 mg/dL.

or

HbA1c $> 6.5\%$
[glucose + globin]

ACUTE COMPLICATION of DIABETES

DIABETIC KETOACIDOSIS

Type-1

① RBS = 250 - 600 mg/dL

② Ketone Bodies

→ Blood

→ KETONEMIA

(Reliable)

→ Urine

→ KETONURIA

(Best Bedside)

③ ↓ pH

C/F

1) nausea, vomiting (persistent)

K.B. (+) CTZ

2) Abdominal Pain ± Tenderness

3) ↑ HR

4) ↑ RR [KUSMALL BREATHING]

Metabolic acidosis → Resp. alkalosis

 $\text{CO}_2 \rightarrow \begin{cases} \uparrow \text{acidosis} \\ \downarrow \text{alkalosis} \end{cases}$

5) Fruity odour → due to acetone

6) **Dehydration** (severe)
M/c of mortality**Rx** -

1) I.v. fluids (4-6 L)
 ↓
 Most effective Rx: 0.9% NS → To prevent ↑ Na⁺, ↑ Ca²⁺ 4-6 hr → **0.45% NS**
 ↓ To prevent hypoglycemia → **5% Dextrose** (RBS < 200)
 x RL x

2) Insulin

Regular → 10 units IV Bolus

↓
0.1 U/kg/hr

3) KCl @ 20-40 meq/hr.

4) NaHCO₃

pH < 7.

HYPEROSMOLAR NON-KETOTIC COMA

TYPE=2

RBS = 600 - 1000 mg/dL

↑ Sx. Osm.

KB ⊖

Altered sensorium

Rx = 1) IV fluid (6-10L)

2) Insulin

CHRONIC COMPLICATION

DIABETIC NEUROPATHY

(A) POLYNEUROPATHY

Distal Symmetry sensory
(M/C type)

glove }
stocking } ⊖ Loss

1st ⊖ lost

Vibration

[128 Hz Tuning Fork]

PARAESTHESIA



ANAESTHESIA

Rx

1) Improved Glycemic control

2) Pain L

AED = Pregabalin

TCA = Amitriptyline

② MONONEUROPATHY

M/c Cranial N/V

III > VII

[Pupillary
sparing]

Mononeuritis multiplex = Patchy involvement of

↳ M/c/c - metabolic = DM [② in India + world]

Infective = LEPROSY

Vasculitis = POLYARTERITIS NODOSA

③ ~~AUTOIMM~~ AUTONOMIC NEUROPATHY

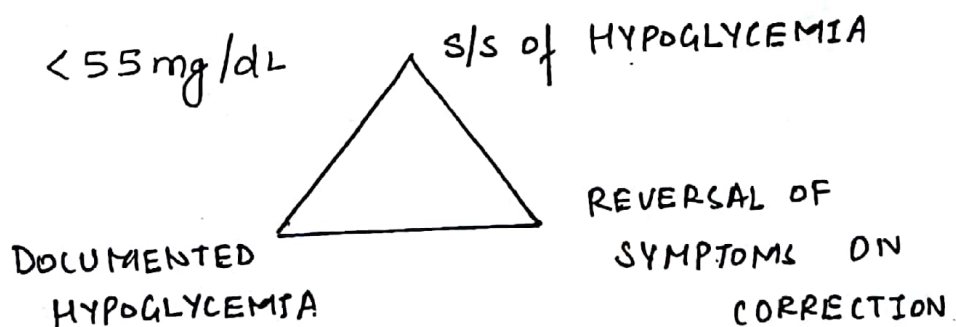
Hypoglycemia Unawareness

β -cell avoided in diabetic pts.

Intensive control is avoided \Rightarrow ↑ Risk of hypoglycemia

HYPOGLYCEMIA

WHIPPLES TRIAD



- 1) ↓ Insulin
- 2) ↑ Glucagon
- 3) ↑ cortisol
epinephrine
GH

EXTENSIVE FASTING x 72 hours

↓
↓ GLUCOSE

↓
↑ INSULIN

↑ Insulin ↑ C-Peptide

HYPER-INSULINEMIA

Only ↑ Insulin

ENDOGENEOUS

EXOTHERMUS

Insulinoma → Radiological

Sulphonylurea Induced

↳ SV Levels

Insulin: glucose $\rightarrow 0.3$

SOMOGYI EFFECT

(40) 3-5 A.M. Hypoglycemia [↑ night Insulin]

counter regulatory hormones

240 8 AM Hyperglycemia

R_x = Long Acting Insulin.

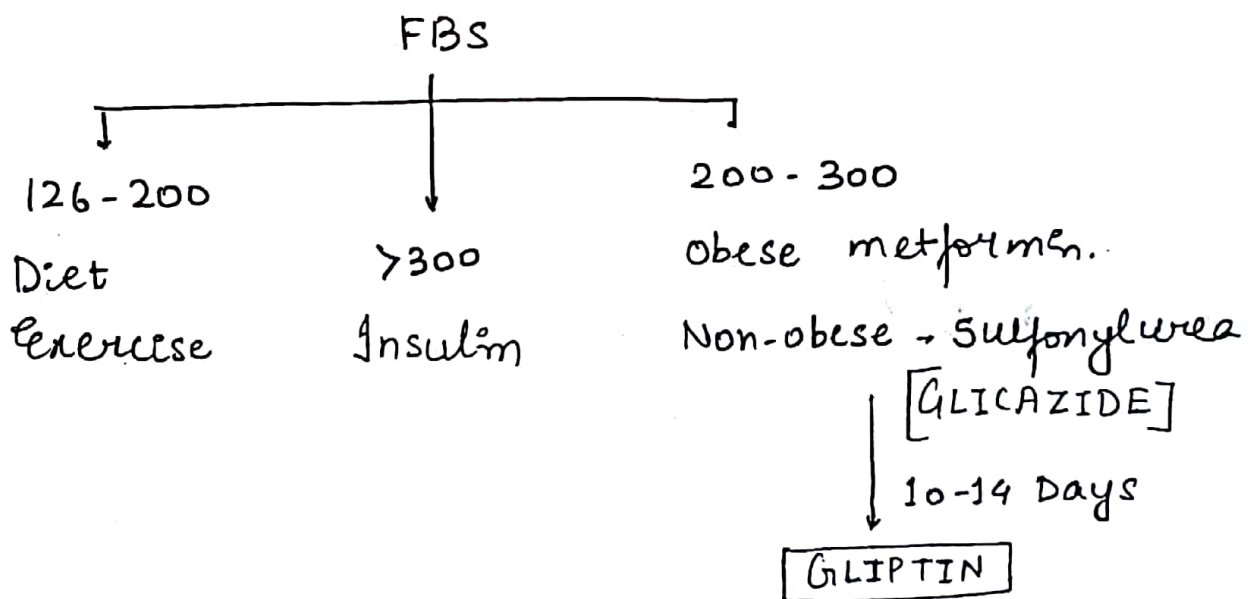
DAWN PHENOMENA

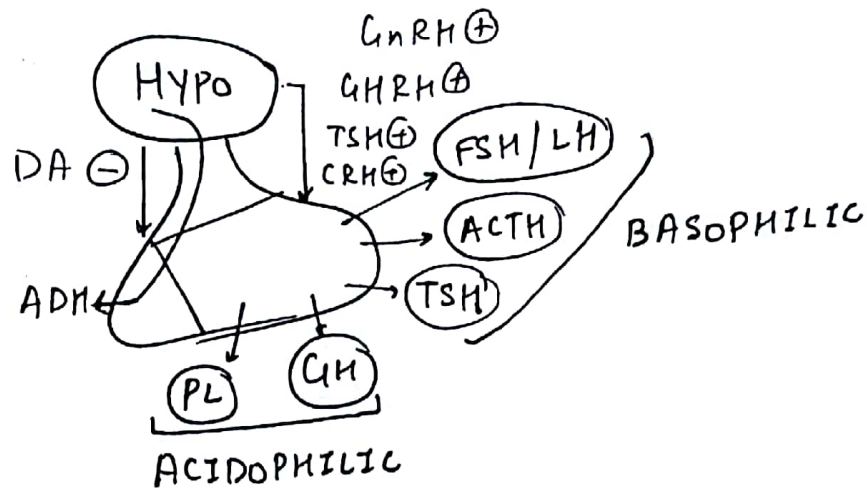
(240) 3-5AM Hyperglycemia
 ↳ Insulinopenia
 ↳ Insulin resistance

(340) 8AM Hyperglycemia

Rx = ↑ night Insulin + Insulin sensitizer

Rx of TYPE-2





STALK LESIONS

↑ Prolactin

Hypothyroidism (central)

↓ glucose

↓ BP

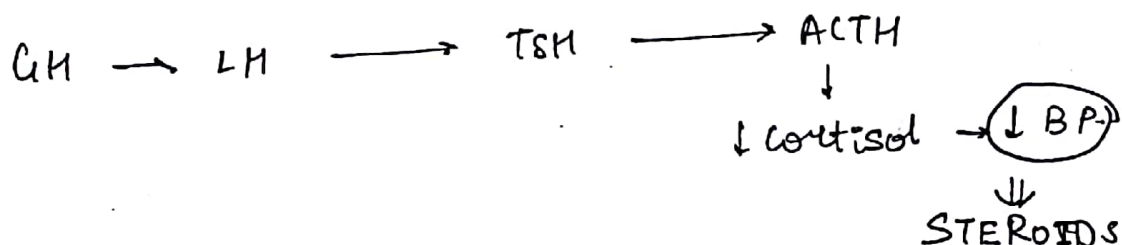
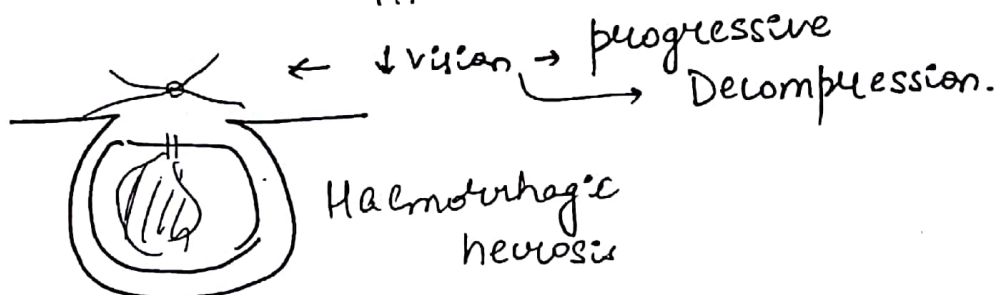
Central DI

PITUITARY APOPLEXY

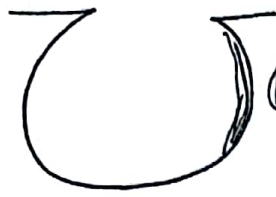
↳ SHEEHAN SYNDROME

↑ Incidence = Sickle cell Disease
DM
HTN

Predisposing Factors



↓
after few months



⑤ functioning Pituitary

EMPTY SELLA SYNDROME (Incidental finding)

MEDICINE (GIT)

427

Liver

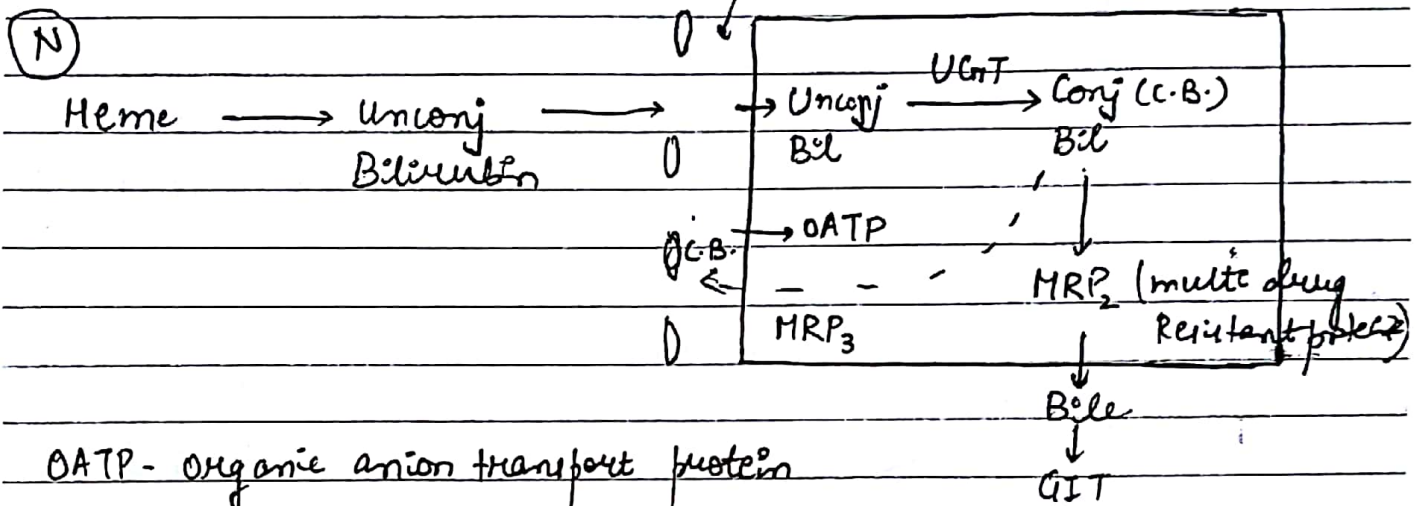
Intestine

- * Disorder of Bilirubin met
- * Acute Viral Hepatitis
- * Chr. hep / cirrhosis
- * Comp. of liver failure

- * Malabsorption syndrome
- * Diarrhoea
- * GI infect
- * IBD
- * IBS

BILIRUBIN METABOLISM

space of Disse



DISORDERS OF BILIRUBIN METABOLISM

I ↑ Unconjugated Bilirubin

1) Increased synthesis-

- a) Hemolytic anaemia → ↑ premature destruction of RBC in periphery
- b) Ineffective erythropoiesis → ↑ premature destruction of RBC in Bone marrow

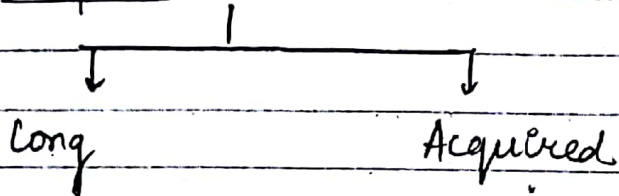
Causes

- Thalassemia
- Megaloblastic anaemia
- Severe Fe def.
- Pb poisoning

c) Large haematoma

d) Lobar pneumonia (\uparrow RBC destrucⁿ in exudate)

II) \downarrow Uptake :-



Gilbert Syndrome-

Drugs- Rifampicin

Probenecid (prophylaxis for gout)

Ribavirin (for Hep C virus)

3) \downarrow UGT :- (UDP glucosyl transferase)

* Cong. causes-

Crigler Najjar I

CN II

Gilbert Syndrome

UGT activity	0%	10%	33%
--------------	----	-----	-----

Mode of inheritance	AR	AR	Both (AR & AD)
---------------------	----	----	----------------

S. Bil (Total)	>20	6-20	<4
----------------	-------	------	------

Kernicterus	(+)	Rare	(-)
-------------	-----	------	-----

Mortality	Before 1 year @ 20% t/t-	Adulthood	Not \uparrow .
-----------	--------------------------	-----------	------------------

Inv

	CNI	CNII	Gilbert Syndrome
<u>Inv</u>	N	N	Lipofuscin pigment
Liver B _x			= Brown colour

R _x	Liver Transplant	Enzyme inducer	No T/t Needed
----------------	------------------	----------------	---------------

Phenobarbital



25% ↓ in S. Bil.



If no response then
go for Liver Transplant

* Acquired causes :-

1) Drugs - Gentamicin
Chloramphenicol
Pregnanolone

2) Breast Milk Jaundice (Self-Limiting)

FA ⊖ → UGT of neonate →

No need to stop feeding

3) Lucey Driscoll Syndrome :- (Self Limiting)
Maternal serum Ab ⊖ UGT of neonate

(II) ↑ Conjugated Bilirubin (Isolated).

Liver enzymes (N)

Dubin Johnson Syndrome

Rotor Syndrome

Mech. ⊖ Mutation of MRP_2

⊖ Mutation of $OATP$

Mode of inheritance AR

AR.

S. Bil. < 4

< 4

Kernicterus ⊖

⊖

Mortality not ↑

not ↑

Inv

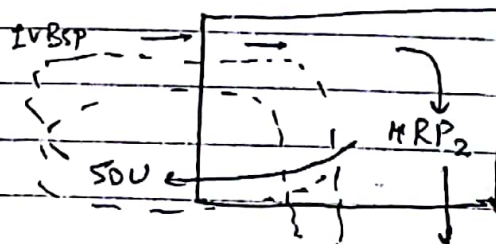
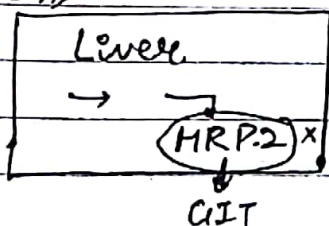
Liver B_x Black Pigmentation.
(Epinephrine metabolite (N)
excreted by MRP_2)

Normal.

BSP clearance test

(Brom sulphalein)

I.V. BSP →



(N) BSP clearance ≤ 90 min

∴ MRP_2 absent, hence no clearance of BSP

Delayed clearance of BSP

R_x not Req

Not Req.

Q. 2 feature will suggest cause of ↑ of unconjugated Bil except :-

a) GB pigmented stones (H. anaemia) True

b) P/s → spherocytes (H. anaemia) True

c) Acute hep C viral infection Enzyme ↑ + conj. bil. ↑

d) H/o gout. True (Probenecid)

ACUTE VIRAL HEPATITIS

caused by hep A to E

Hep A

① Mode of - H/c Feco-oral
Transmission.

② Transmission to - common
close contact

③

③ Rare - • Blood Transfusion
Viraemia during late
incubation period

• Sexual

④ Not a mode
of transmission Vertical

Hep E

H/c Feco-oral

sewer line

Rare

community
spread.

'New epidemic in
community'

Vertical

BT

Sexual

Hep A

Hep E

C/E M/c cause of Ac. Viral Hep. in children.

M/cc of Ac. Viral Hep. in adults.

[M/c of Viral Hep - B]

M/cc of Ac. Viral Hep. in
♀

[M/cc of Viral Hep in ♀ = B]

Relapsing Hepatitis
2 clinical episodes by same virus in ac. phase (< 6 months)

Cholestatic hepatitis.
swollen hepatocytes cause obstruction to intrahep. Bile flow.
[ALP also ↑].

Inv

Serology IgM Anti HAV
= Acute Hep. A infectⁿ
IgG Anti HAV - Pt is immune

IgM Anti HEV
= Acute Hep E infectⁿ

IgG Anti-HEV - ~~is~~ Pt is immune

Possibilities.

- Post vaccination ✓
- Remote recovered past infectⁿ ✓
- Chronic infection - X
(virus ⊕ > 6 months)

±

✓

X

Complications.

1) Fulminant hepatitis - 0.1%
(encephalopathy < 2 wks of Jaundice)

~~♂~~ non ♀ → 1-2%
♀ → 10-20%

2) Chronic Hep	0%	0%
(Viral i +ve. for >6mths + Liver damage ⊕)		
3) Carrier	0%	0%
(Virus + >6mths Liver damage ⊖)		

LMP Topic

Hep B

Mode of Transmission ① M/c - vertical

Mother HbeAg ⊕



Risk - 90%

Anti Hbe Ab



Risk - 10%

Hep C

① M/c - Percutaneous

Needle



1.8 - 6%
Risk

>

BT

1 in 18 Lacs of
Blood units

Viable < 4 days

transfused

② Percutaneous

Needle

6 - 30% Risk

viability of virus
7 days

M/c BT related virus = (B)

BT

1 in 2 Lacs of
BU transfused

MOT

Needle

accidental

BT

HIV

Injecting

Risk

0.6%

0.3%

1 in 22 Lacs

(Some donors have low level HBsAg & it NOT detected by routine lab method).

NOT

HIV

Risk

Vertical - 5% risk

③ Sexual variable

Sexual 5% risk

Rare. NOT

Secreted into saliva = yes
Human Bite yes

yes.
yes.

Not NOT

• Virus secreted into ~~st~~ stool yes

yes.

• Feco - oral transmission

No

No.

(destroyed in stomach)

• Breast milk secreted yes

yes

• " " transmission No

No

• Secreted:

Q. All are transmitted by blood except

a) Hep A

a) Hep A

a) Hep A

b) B

b) B

b) B

c) C

c) C

c) C

d) E

d) HIV

d) G

Q. All causes AVH, transmitted by blood except

a) Hep A

b) B

c

d) G. → never causes AVH.

Q. M/c mode of transmission of hep B

1) Vertical vs Horizontal

2) Vertical vs Percutaneous vs Sexual vs Human Bite

Q. Hep B not transmitted by

a) saliva

b) semen

c) Few-oral

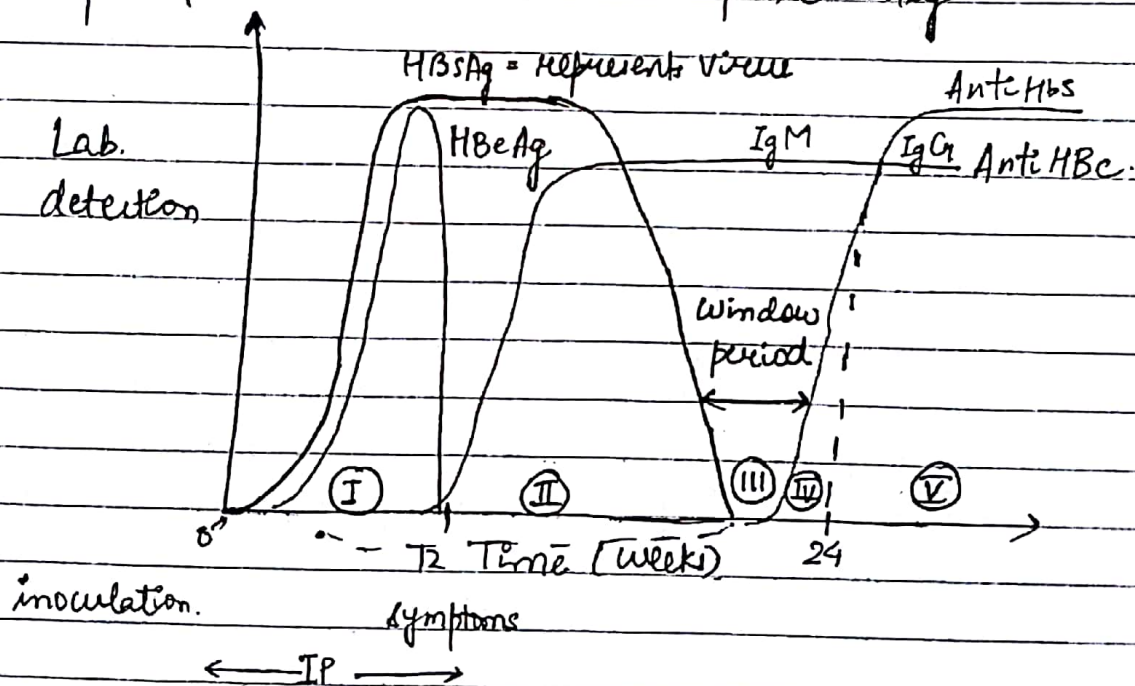
d) Breast feeding.

Q/F	Hep B	Hep C
	Mcc of viral cause of HCC	Mcc viral cause of cirrhosis
	↓ express HBsAg	[Mcc of cirrhosis = Alcohol]
	⊖ p53	⊕ Viral Replication
	Mcc viral cause of chr. Hep = (Prevalence wise)	Mcc AVH leading to chr. Hep. or
		Max. Risk of chronicity
	Mcc of Carrier	

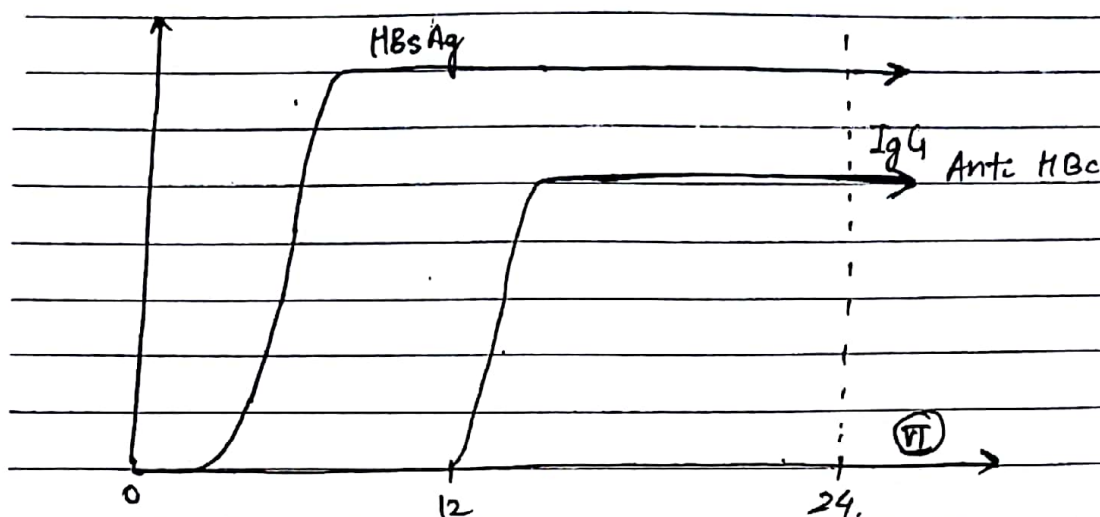
Serum sickness like illness \downarrow HBsAg + Ab Joint pain + rash In children = LN + Hepatosplenomegaly + Rash Gianotti Cresti Syndrome	Insulin Resistance by \ominus Insulin action \uparrow Risk of T ₂ DM
---	---

* Serology of Hep B Infection

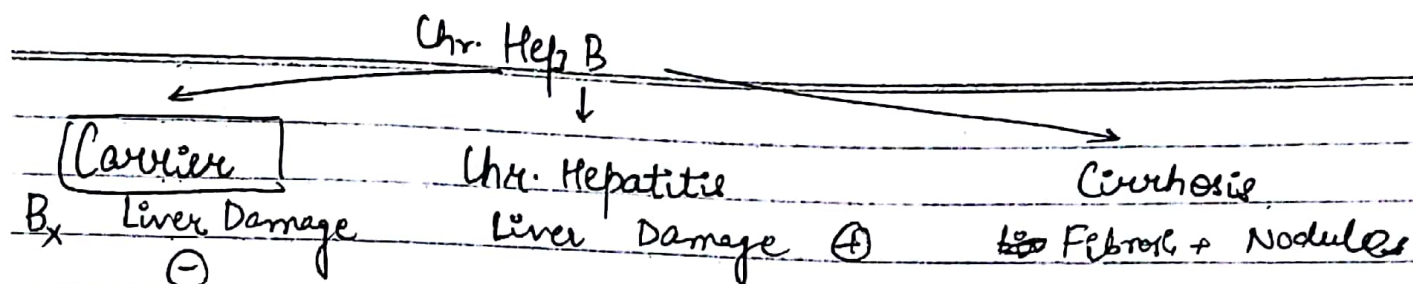
1) If Hep B limited to Acute phase only



2) If hep B converted to chronic infection



Phase	Marker
① I.P.	HBsAg, HBeAg. Earliest marker of HBsAg.
② Acute (symp) Hep B infection	HBsAg, IgM Anti HBc Most reliable marker of Ac Hep B infection.
③ Window period	IgM Anti HBc
④ Recovery period of Ac. Hep B	IgM Anti HBc, Anti HBs
⑤ Remote past infection	IgG, Anti HBc, Anti HBs \pm (disappears after yrs)
⑥ Chronic infection	HBsAg + IgG Anti HBc.



HAI (Histological Activity Index) ≤ 3

≤ 3

> 3

Active

Replication (+)



DNA copies.

$> 1000 / \text{mL}$

Inactive.

(-)

$< 1000 / \text{mL}$

Replication markers:-

1) Quantitative marker \rightarrow DNA copies \leftarrow Most reliable replication marker

2) Qualitative marker \rightarrow HBe Ag.

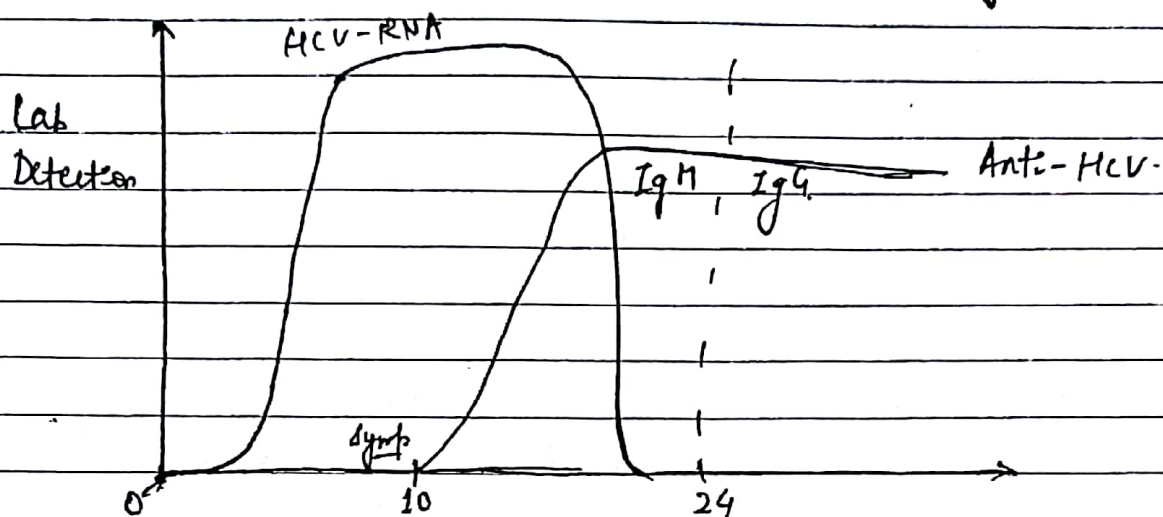
Exception Pre core Mutants of hep B virus

↓
Unable to make HBe Ag but
replication (+)

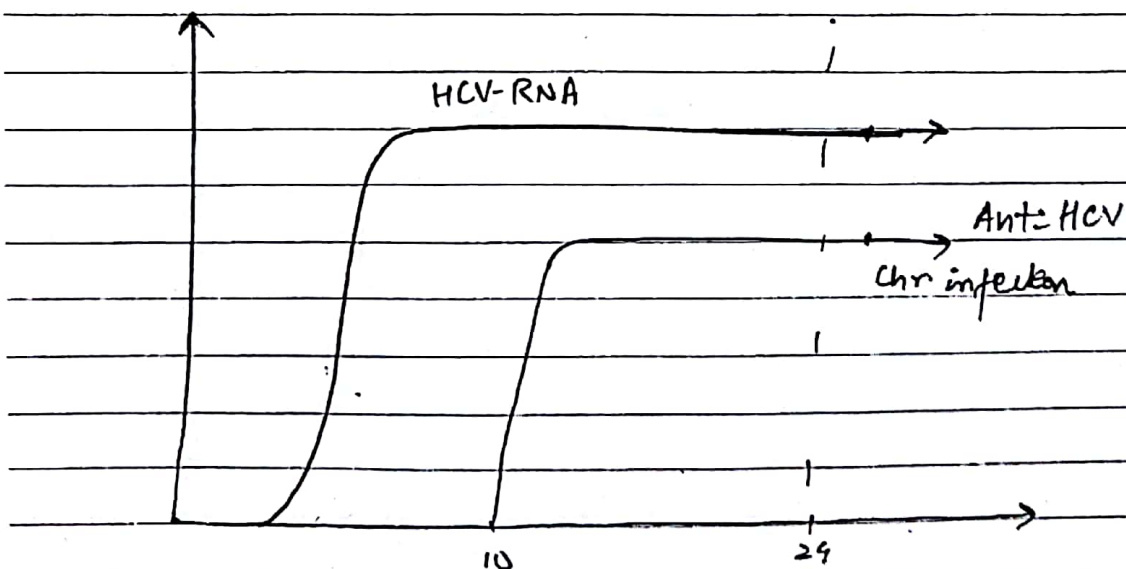
	DNA	HBe Ag	Δ
①	(+)	(+)	Replicative phase of hep B virus
②	(+)	(-)	Pre-core mutants of hep B
③	(-)	(-)	Non-replicative phase

* Serology of Hep C Infection :-

1) If Hep C limited to Acute phase only.



2) If Hep C converted into chronic infection.



- ② Chr. Hep } → depend on Hep B.
 ③ Carrier }

T/t

① AVH

→ Supportive care (mostly self limiting).

↓
 Iv. fluid of choice = Dextrose as hypoglycemia risk.
 Min. Dextrose Req. = 150 g/day.

If 5% Dx = 3000 mL/d
 (5g/100mL)

If 10% Dx = 1.5L/day → Fluid of choice

If 25% Dx = 600 mL/day. → may cause thrombophlebitis.
 ↳ not used for maintenance
 reserved for emergency

2) Antivirals.

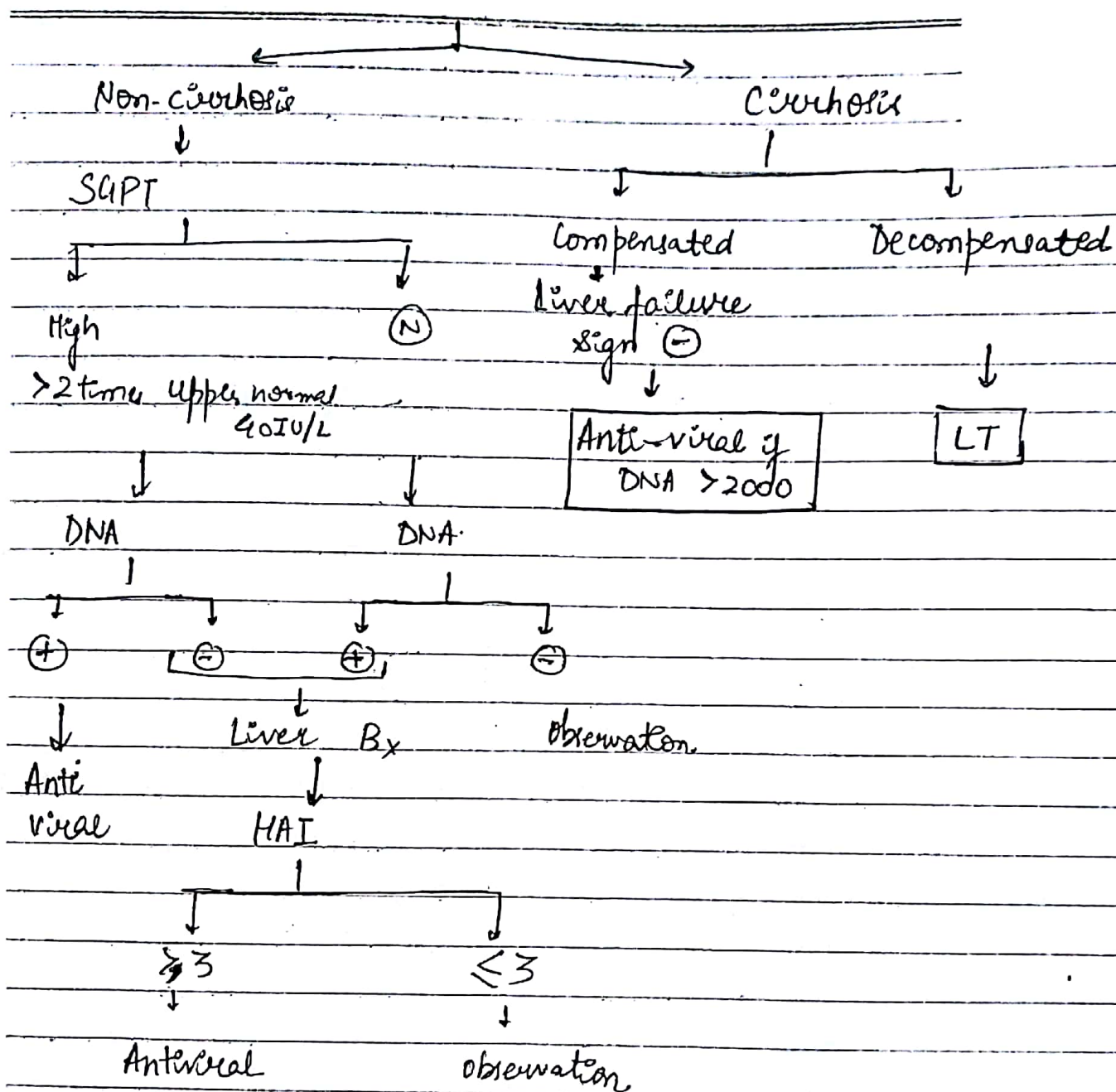
for Acute Hep C

↓
 Interferon α . 12-24 wks

LMP Topic

II Chronic Viral Hepatitis

Approach to Chr. Hep B infection



DNA is (+) pre Anti-viral if $\geq 20,000$ IU/mL in HBeAg (+)
 if ≥ 2000 IU/mL in HBeAg (-)
 (Pre-core mutants).

Anti-viral for Hep B

① Initiate = Monotherapy from 1st Line agents

1) Interferon α -

- oldest
- Less effective in Cirrhosis

2) Entecavir -

- Most potent
- ↓ effectiveness in lamivudine resistant cases

3) Tenofovir → DOC.

- Safest & effective even in Lamivudine (R) cases

Duration ≥ 1 yr

② Chre. Hep. C Infection

Non-Cirrhosis



Start Anti-viral if

- 1) HCV-RNA detectable
- 2) Bx - mod-sev hepatitis
[HAI > 3]

Cirrhosis
(Fibrosed)



Compensated



Anti-viral



De-compensated



LT

Antiviral for Hep C

Initiate = Dual therapy (oral combination therapy)

INF α → outdated. nowadays

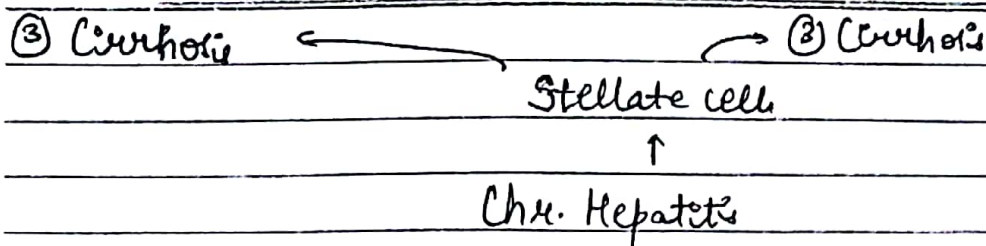
Sofosbuvir + Velpatasvir → effective in all 6 genotypes.

Sofosbuvir + Daclatasvir

Duration - 12 wks. for all genotypes.

FATTY LIVER

Alcoholic Liver Disease	Non-Alcoholic Liver Disease
<u>Patho</u>	
Dose → 40-80 g/d = fatty liver 80-160 g/d = cirrhosis Duration 10-20 yrs	Dose of alcohol → 0-20 g/d.
♀ → Dose is half.	cause - Insulin Resistance
<u>Stages</u>	<u>Stages</u>
① Fatty Liver	① Fatty liver
Ethanol	<u>Mech.</u>
↓ ⊖	TG deposit
② FA metabolism	Insulin Resistance
↳ ↑ free FA → (↑ TG)	↑ TG.
TG deposit	Lipolysis → ↑ free FA
② Hepatitis ← TNFα	② Hepatitis ← oxidative injury
F.L + enzymes ↑	



C/F

1) Peripheral Neuropathy

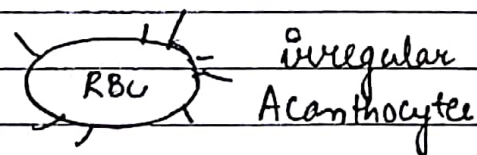
↗ direct alcohol effect ↖ Pure sensory
Pyridoxine def. induced by alcohol

1) Causes of Insulin Resistance

- ① M/c obesity
- ② Type 2 DM
- ③ Steroid (⊖ insulin action)
- ④ Hep C

2. Zieve's Syndrome⁸⁰

Deep Jaundice due to additional effect of haemolysis induced by alcohol



Q. C/F suggest alcohol as a cause of cirrhosis

- ② Spider angioma due ↑ oestrogen → ↓ catabolism in Liver
- ③ Gynaecomastia
- ④ Loss of deep tendon reflex
- ⑤ ascites.

Ix

① $\frac{SGOT}{SGPT} > 2$ Highly specific for ALD

① $\frac{SGOT}{SGPT} \leq 1$

(SGPT synthesis need pyridoxine)

② γ GT - \uparrow

Site = Bile duct + (ER)

Fat Squeezes ER to release γ GT.

③ Peripheral Neutrophilia (+)

TNFA recruits

if neutrophils $> 5500/\text{mm}^3$
= Poor Prognosis

Rx.

① Fatty Liver. = Reversible after
cessation

② Hepatitis Doc - Steroid
act on TNFA.

Indication if MADREY's
alcoholic discriminant funcⁿ > 32

$$= 4.6 \times \left[\frac{\text{PT of pt.} - \text{PT of control}}{12 \text{ sec}} \right] + \text{S. Bil}$$

③ Cirrhosis

Best Rx \rightarrow Liver Transplant

Recurrence of 1^o disease

after LT = Nil if underlying cause Remains treated

③ γ GT - \uparrow

(-)

FL = Reversible \rightarrow Rx of underlying
cause \rightarrow obesity

Vit E.

\downarrow act as Anti-oxidant

Cirrhosis

Liver Transplant

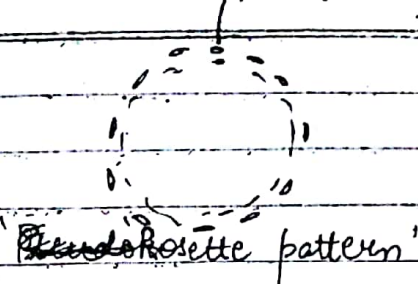
AUTOIMMUNE

447

↓		↓	
Autoimmune Hepatitis		1° Biliary Cirrhosis	
Patho		Autoimmune fibrosis of intrahepate Bile duct	
Direct Ab damage to the hepatocytes. (Type II HS)		↓ Bile accumulation ↓ Damage hepatocytes	
C/F		♀	
♀		♀	
Age		40-60 yrs	
20-40 yrs			
Recurrent (recur over years)		Pruritus Xanthelasma (cholesterol deposit in the eyelids)	
Inv Ab depends on type of		M/C / Most sensitive / Most specific	
AIH		M/C	
ANA I - M/C → ANA Most sensitive		Ab → Anti mitochondrial Ab	
A			
Ab → Smooth ms cell			
P-ANCA			
(II) → Anti LKM (Liver kidney microsome)			
↓			
(also +ve in Hep C infection)			
(III) → Least common, most severe			
Ab → Liver soluble antigen			
Most specific			

Regenerating
hepatocytes

B_x



Non-suppurative inflammation/fibrosis
of intrahepatic Bile ducts

R_x
① Hepatitis = Steroids (Doc)

① Compensated cirrhosis
Ursodeoxycholic Acid (UDCA)
(solubilise bile to non toxic)

② Cirrhosis
Decompensated → LT

② Decompensated cirrhosis
LT.

Recurrent after LT →
(common upto 50%)

Recurrence after LT → rare

LMP Topic

GENETIC

WILSON'S DISEASE

Patho AR mutⁿ of
ATP7B
↓
↓ Cu excretory protein
in liver
↓
Cu overload in the body

CF Liver Most common
organ

age < 20yr

Chr. Hepatitis +


HAEMOCHROMATOSIS

AR mutⁿ of
HFE
↓
↓ Heparin [↓ Fe absorpⁿ]
↓ ↑ Fe absorption
Fe overload

Liver

> 40yr

+

Etiology: Macronodular	Mixed or Micronodular
HEC +	++ (M/c cause of death even in t/t.d. pt.)
2 nd organ affected CNS ↳ Basal Ganglia	CNS ↳ Hypothalamic pituitary axis
M/c CNS manifestation Thromb.	Hypogonadism
Frontal lobe ↳ neuropsychiatric abnormalities.	
Cr. N/v → XII th (M/c Cr. N/v affected) (Dysarthria)	
Autoimmune dysfunction. ↳ Postural Hypotension.	
Not affected → 1. Sensory system 2. Motor power. (Pyramidal pathway)	
3 rd Colour Change Eyes	Skin.
↓ daytime vision = sunflower cataract	due to Fe + melanin deposits
Kayser-Fleischer Ring (Vision (N))  Peripheral	↓ Bronze Pigmentation.

④ Functional Effect

Kidneys
 ↓
 Proximal Tubular Dysfuncⁿ
 ↙ ↘
 RTA - 2 Fanconi Syndrome

Pancreas

β cells affected

↓
 Broome DM.
 ↓
 * Reversible after t/t of
 haemochromatosis unless other

⑤ Structural Damage

RBC Membrane

↓
 Haemolytic AnaemiaJoints (2nd & 3rd MCP jt)↓
 Fe in joints ⊖ Pyrophosphatase↓
 Ca Pyrophosphate ↑↓
 Pseudogout

⑥ x

CVS - Fe infiltrate inside
 myocyte↓
 Myocyte
 Contraction ↓↓
 Myocyte relaxation ↓↓
 DCMP↓
 RCMP
 DCMP > RCMP
 M/c cause of death ⇒ CVS
 in untreated pt.

Inv

 (15) Free Cu + Apoceruloplasmin
 Ceruloplasmin (Bound Cu)

Ab(N) ↓ binding of free Cu ²⁺ apoceruloplasmin	1. S. Fe → ↑ 2. % Transferrin → ↑ saturation
1. S. Free Cu → ↑ 2. S. ceruloplasmin → ↓ 3. S. Total Cu = ↓ (mainly in bound form)	3. S. Ferritin ↑ 4. TIBC ↓ 5. ^{New} UIBC ↓↓ = TIBC - S. Fe (unsaturated) ↓ ↑ ↑ Most sensitive Inv
4. Urinary free Cu levels - ↑	
5. Bx - Liver Cu > 200 µg/g dry liver wt.	6. Bx → ↑ Fe. Prussian Blue Stain
R _x D Hepatite → Zn (DOC) [50mg tds] ↓ ⊖ Cu absorption	Hepatitis → R _x OC → Phlebotomy • 1mL Blood will remove → 0.5mg Fe • Single phlebotomy → 500mL Blood. (250mg Fe removed) • Fe overload > 20g ↓ 80 phlebotomy Req.
2) Cirrhosis - According to NAZER SCORE • SGOT • S. Bil • PT. ↓ <7 7-9 >9	Cirrhosis → Liver Transplant Recurrence after LT → rare < 1%
Zinc + Therapeutic Recurrence after LT → NIL	LT pt. will be lifelong Zn therapy

Q. \subseteq causes \uparrow Cu in Liver \rightarrow KF Ring -

- autoimmune cholangitis
 - 1° Biliary cirrhosis
 - 1° sclerosing cholangitis
- At All

Ch4. Cholestasis condition

Q. After Phlebotomy manifestation of haemochromatosis?

Reversible

- Hepatomegaly
- Skin pigmentation
- Diabetes
- CHF

Irreversible

- Cirrhosis
- Arthritis
- Hypogonadism

Q. HFE mutation \uparrow risk of \subseteq cancer = Breast
Colon Cancer

COMPLICATIONS OF LIVER FAILURE

1) HEPATIC ENCEPHALOPATHY

Mech - \downarrow urea cycle

\downarrow
 \uparrow NH_3

Astrocyte Damage

C/F - West HAYE's Grading

Restless I Earliest symptom = altered sleep cycle
 " sign = altered handwriting (constructional apraxia)

Drowsiness II

Trail making test

Stupor III

join to ① to ②⑤ numbered circles

(N) time 15-30s.

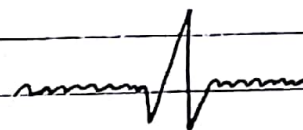
Coma IV

Deep coma V

Inv

EEG → ① most characteristic

Triphasic large
amplitude wave
(Grade II to IV)



② S wave - Grade V
(1-4 Hz)



Rx

▷ Rx / ppt cause

Mech.

Rx

① GI infection

↑ bacterial proliferation

Ab of choice

the Relaximin.
(550 mg BD)

② upper GI bleed
(ruptured oesophageal
varices)

Blood protein
↓ reach
gut bacteria
↳ ↑ NH₃

If vital stable → Ryle's tube
aspiration.

Rx OC → Endoscopic Band
Ligation of Varices

DOC → Octreotide

2° prophylaxis - β blocker
(never in acute bleed)

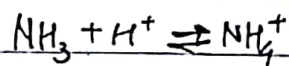
③ $S \cdot K^+ \downarrow$

\downarrow Peristalsis
 \downarrow

I.V. KCl infusion
10-20 mmol/hour.

\uparrow Bacterial Proliferation

④ Metabolic
alkalosis



(toxic) (non-toxic)

Rx underlying cause

\uparrow
vomiting
(KCl loss)

if pH \downarrow → eq. shifts to (R)
if pH \uparrow → eq. shifts to (L)

⑤ Constipation

Bacterial proliferation \uparrow

Laxative of choice 2
Lactulose

cause acidic pH.

\downarrow

Target 2-3 stools/day
otherwise may cause diarrhoea

⑥ Hypovolemia

\uparrow Renin → \uparrow aldosterone

CI → RL

\downarrow

Lactate

$S \cdot K^+ \downarrow$

Liver

Met. alkalosis

HCO_3^-

Met. alkalosis

So, IV. fluid → NS

2) ASCITES

* Mech. \uparrow Sinusoidal pressure (compression by nodules)

+
Na & H₂O retention

\uparrow NO synthase (① degraded in liver)

\downarrow NO

Systemic vasodilatation
(Blood pooling in systemic circulation)

Aldosterone \uparrow

Renin \uparrow

Pulmonary vasodilatation

Renal perfusion \downarrow

Hepato-Pulmonary Syndrome

Hepato-Renal Syndrome

* C/F

Min

Sign

PUDDLE

Min fluid needed

120 mL

Shifting dullness

500 mL

Fluid thrill

1500 mL

* Inv

Ascitic fluid

• Preferred site \rightarrow ① lower quadrant

• Needle Size = Diagnostic 20-22 G
Therapeutic 15 G

Umbilicus

$\frac{2}{3}$

$\frac{1}{3}$

ASIS

Step ① S. albumin - Ascitic Albumen (SAAG)

<1.1

(↓ Sinusoidal pressure)

- 1) ↓ S. albumin ↓
eg. Nephrotic Syndrome

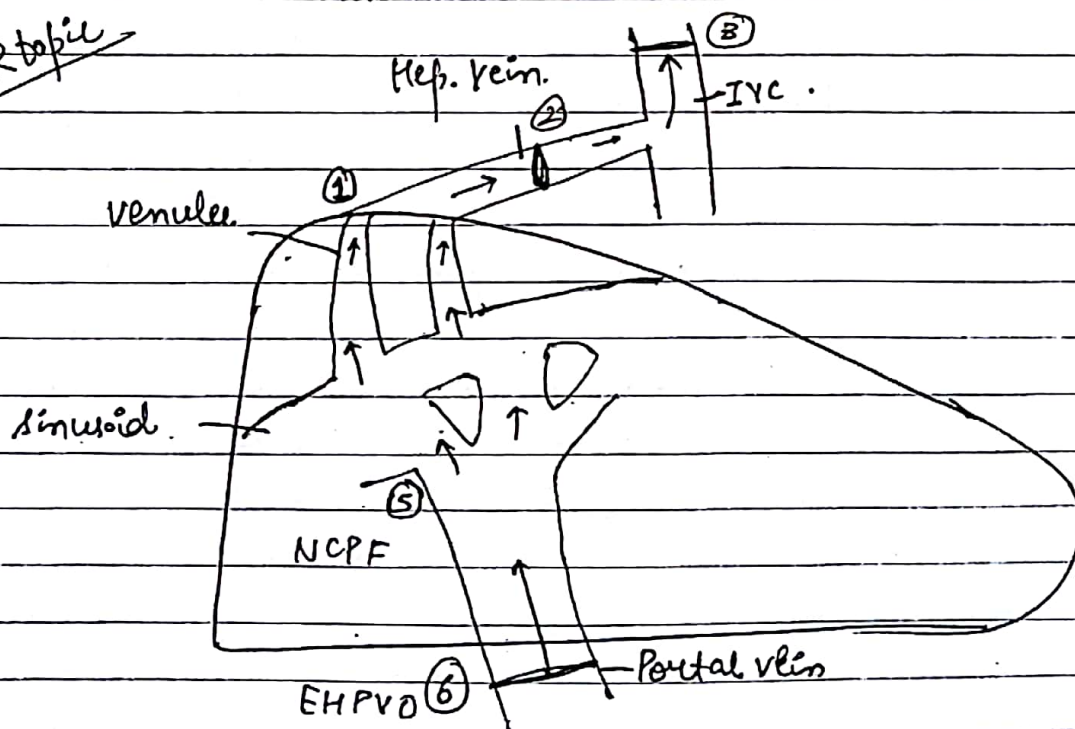
- 2) ↑ Ascitic albumin ↑
due to ↑ Peritoneal vessel permeability

eg. TB peritonitis
Cancer

Acute Pancreatitis

Heart ④

LHR topic

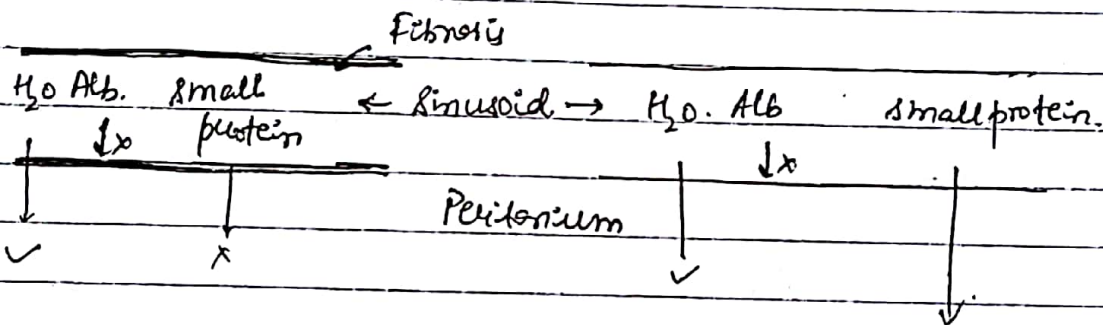


Step 2 - Ascitic Total Proteins \leftarrow if SAAG > 1.1 .

Cirrhosis
 < 2.5

Non-cirrhotic
(Post-sinusoidal obstruction)
 > 2.5

- ① Ven-occlusive Disease
- ② Budd. Chyari
- ③ IVC obstruction
- ④ CHF / Constrictive Pericarditis



Rx
Grade
I = Mild Ascites

Defⁿ
No clinical signs

Rx
salt restriction

II = Moderate "

Clinical signs +ve
Respiratory distress -

Add diuretics
spirolactone
(max - 400mg/day)

Furosemide
(max - 160 mg/d)

III. Severe

Resp. Distress +

Large vol. paracentesis
(5-6L removed)

+

I.V. albumin
(to retain intr. fluid)

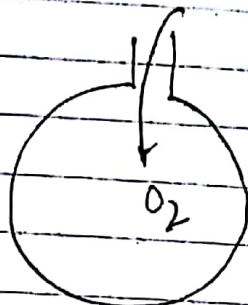
IV Refractory Ascites	No response > 7 days of Max dose of Both diuretics	Same as Grade III
--------------------------	---	-------------------

⑤ Non-Cirrhotic Portal Fibrosis	⑥ Extra-hepatic Portal vein Occlusion
Age > 20 yr	< 20 yr
c/f upper GI bleed + ↑ Portal HTN + ↓ Spleen + > 7 cm below costal margin	+ + + < 7 cm below costal margin
Jaundice (-)	(-)
Encephalopathy (-)	(-)
Ascites (-)	(-)
Rx - Endoscopic Band ligation +	+

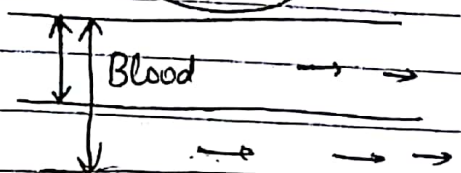
3. HEPATO - PULMONARY SYNDROME.

Mech.

Pulmonary vasodilatation



(N) Pulmonary artery diameter



If vasodilⁿ = diam
occurs increases

mixing \bar{c} deoxygenated blood
on L side

R to L shunt

C/F

Platypnoea - dyspnea ↑ on standing [diaphragm moves down ↓

shunt open ↓

hypoxia ↑]

Inv

① ↓ in O_2 saturation by 3% on standing from supine
Orthodeoxia

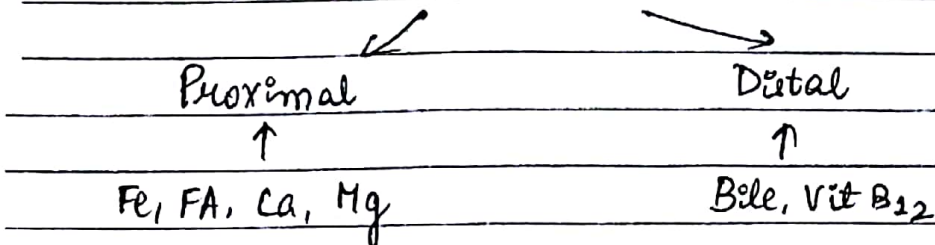
R_x -> Sclerosis of dilated vessel

2) R_{oc} = Liver Transplant

INTESTINAL

MALABSORPTION DISEASES

due to SI diseases



Fat, CHO, Protein ++

+

Tests for malabsorption

I) For Fat :-

- ① Gold std → 72 hour stool fat estimation
if fat excretion > 6% ⇒ Steatorrhea

H/C abnormality seen in ^{any.} malabsorption syndrome

- ② Spot Ix → Sudan III stain.
+ve if stool fat > 10%

II) For Carbohydrate :-

- ① Most specific Ix → Dxylose Test

Cause of < 4.5 gm excretion

1) Pyloric stenosis

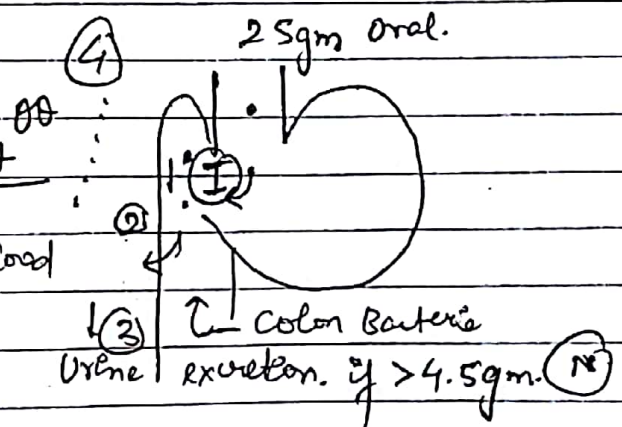
2) Proximal SI diseases

eg. Celiac sprue

3) Bacterial overgrowth Syndrome

4) 3rd space loss → ascites

Pleural effusion



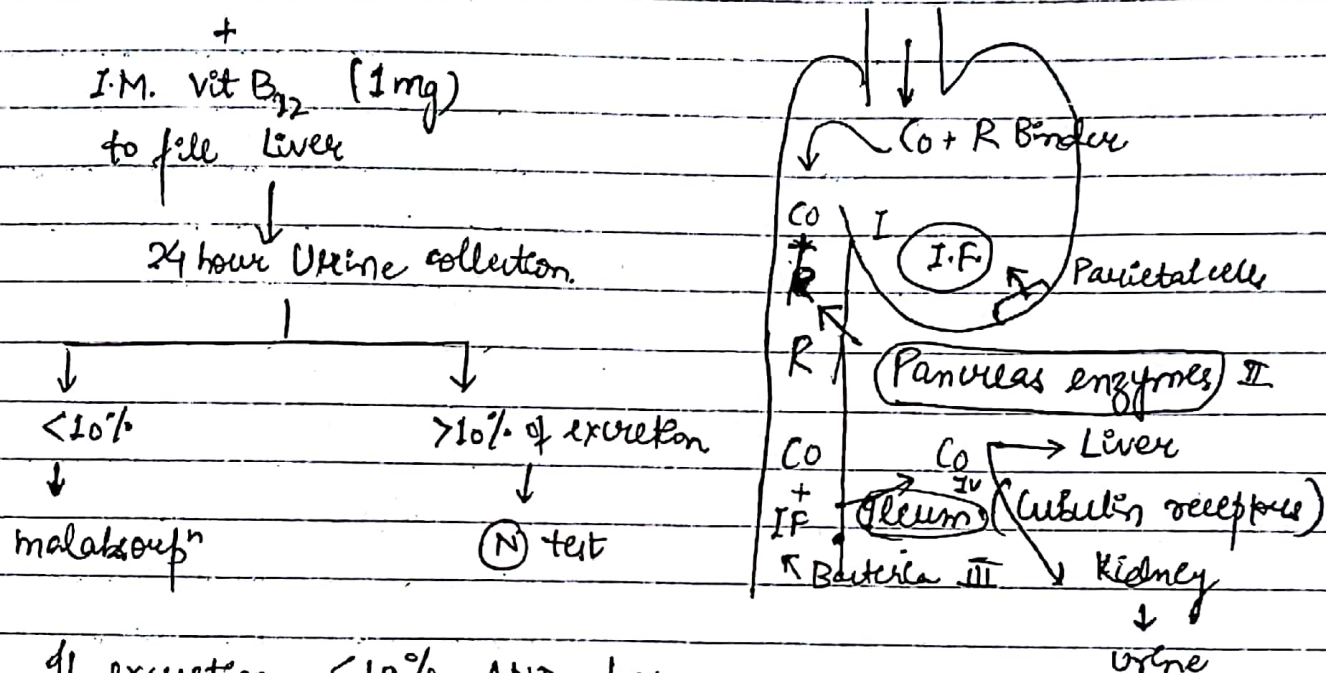
⑤ Renal failure

(III) Vit B₁₂ malabsorpⁿ

SCHILLING'S TEST

① Oral radiolabelled Cobalamine

Cobalamine



If excretion <10% AND becomes >10% after adding.

1) I.F. → Pernicious Anaemia

2) Pancreatic enzyme → Chn. Pancreatitis

3) Ab x 5 days → Bacterial overgrowth syndrome

if remains <10% → Ileum disease

Q. In dietary deficiency of B₁₂, schilling test (N)

Q. Mut' of cubulin (B) \Rightarrow IMERSLUND GRIESBECK'S SYNDROME

IV Intestinal Biopsy

Gold Std. Ix as Most Specific Ix for malabsorption.

Etiologies of Malabsorption-

COLIAC SPRUE	TROPICAL SPRUE.
Cause GLIADIN Hyperensitivity (+ve on gluten) \downarrow Local Contact HS	Bacterial Toxins. + Folic acid deficiency (\downarrow mucosal repair)
Prox SI > Distal SI	Distal SI > Prox SI.
9F* Age - Typical 6-12 months	Adults
Can occur at any age Spontaneous remission = 2 nd decade	
* Steatorrhea (large vol, foul smelling) leading to \downarrow Chronic > 4 weeks. Non-inflammatory (No blood or pus in stool)	✓
* Extra-intestinal manifestation. H/c - Dermatitis Herpetiformis Other - T1DM, IgA deficiency	

COELIAC SPRUE

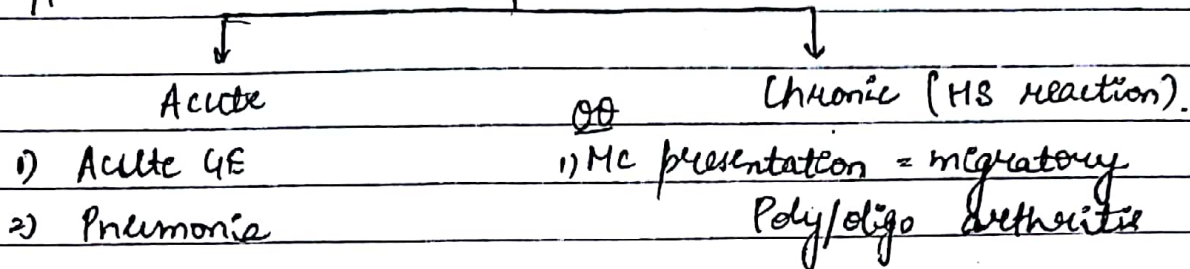
TROPICAL SPRUE

Inv		
① Serology	+	-
Most specific Ab = Anti-Endomysial Ab.		
Most sensitive Ab = Anti tissue Transglutaminase (TTG)		
Most sensitive + specific Ab/Mc/ But = Anti TTG		
② Biopsy		
• Loss of villi	+	reversible after
• Flat mucosa	+	gluten free
• Lymphocyte infiltration	+	diet
③ HLA DQ2 (+) in 100% cases.		
HLA DQ8 but non-specific		
Rx		
1. Gluten free diet		Antibiotics → Doxycycline or Rifaximin.
2. Steroid. Indications		+
1) Refractory sprue		Folic acid.
2) (no response upto 12 months) of gluten free diet		Duration of Ht → 6 months
3) celiac shock (↑ gluten load)		
4) SI Lymphoma		
M/c cause of death		

WHIPPLE'S DISEASE

~~Acc~~ Cause - *Tropheryma whippelii*

CF



2) CNS

M/c → Dementia

Most characteristic CNS manifestation
Oculo Mastatory Myorhythmic

(conv./diverg.)
nystagmus.

Other CNS manifestation

- Cerebellar ataxia
- Myoclonic seizure
- Encephalopathy
- P. Neuropathy

Q. organ not involved in whipple's

- ① Kidney
- ② Lung
- ③ es
- ④ CNS

3) CVS - Pancarditis

M/c - Pericarditis

4) Eye - Uveitis

5) Polyserositis = Ascites
Pleuritis

Inv B_x - PAS +ve macrophage containing

D/D → TB

Bacilli
AFB ⊖

TB
AFB ⊕

R_x ① GIT → ceftriaxone (2wk) → cotrimoxazole (1yr)

② CNS/CVS
(↑ risk of recurrence) → ceftriaxone (2wk) → Doxycycline
+ Chloroquine
or Hydroxychloroquine } 1 year

BACTERIAL Overgrowth Syndrome

Proliferation of colonic bacteria in prox SI

Causes -

↓
Communication betⁿ
LI & SI

↑
fistula

↓
Anatomical stenosis
of SI

↑
structure
* Intusseption

↓
Functional Stenosis
of SI

(↓ Peristalsis)

↑
DM

systemic sclerosis

QF -

1) Steatorrhea

Bile is deconjugated by bacteria in S.I.

Inx

1) 72 hour stool test. >6%

2) D-Xylose Test

excretion <4.5 gm

3) Schilling Test ab (N)

4) S-Folic acid level ↑

(Synthesis by bacteria & reabsorbed by prox. SI mucosa)

5) Lactulose Breath test or H⁺ Breath test.

↓

+ve in Breath 2-8 hour after giving Lactulose as Bacteria in SI metabolise.

6) Endoscopic jejunal aspirate culture

↓

M/C organism E. coli >10⁵/ml

Rx

1) T/t underlying cause

2) Cyclic Ab. antibiotic [Co-amoxyclov.

Ab x 1 week

↓

gap 3 wk

↓

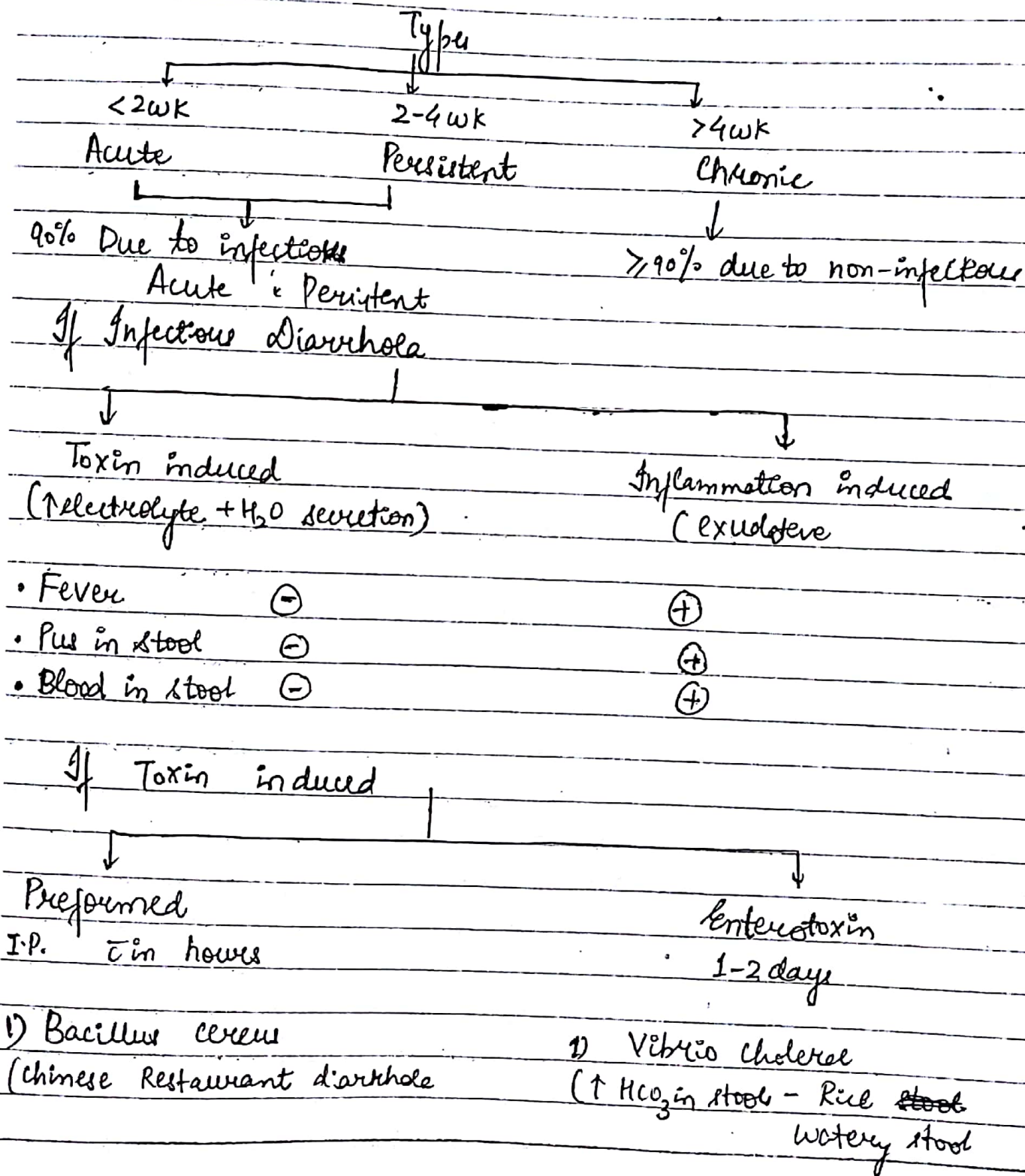
Ab 1 wk

APPROACH TO DIARRHOEA

Essential Criteria for Diarrhoea

Stool vol. $> 200 \text{ mg/d}$
 Stool wt. $> 200 \text{ mg/d}$

Duration.



1) Staph. aureus.

2) Enterotoxigenic E. coli

M/c of Traveller's diarrhoea

3) Clostridium Perfringens

If inflammation induced

I. Mild = mucosa limited. (blood in stool ⊖)

II. M/c viral diarrhoea in adults = Norovirus

" " " Children = Rota virus

II Mod. = submucosa

1) Salmonella → involves ileum

↓

Bile reabsorpⁿ ↓

↓

Bile in stool.

III Severe

2) Yersinia → severe ileum inflammation
Pseudoappendicitis

③
III Campylobacter J. M/c infectious cause of GBS

III Severe = Deep layers

1) Shigella → Toxic encephalopathy
Ehlers Syndrome

2) E. histolytica → flask shaped ulcer

R_x - acute/persistent diarrhoea

① Essential - Rehydration

I.v. fluid of choice → RL contains	mmol/L
K^+	4
Na^+	130
Ca^{2+}	2
Cl^-	109
Lactate ⁻	28
Osmolality	273
slightly hyposmolar	

②

② Antibiotics

Indication - Mod to severe inflammatory infectious diarrhoea

if > 1 of 3 criteria (+)

- Fever $> 101^\circ F$
- Blood in stool
- Pus in stool

Empirical = Fluoroquinolones.

Chronic Diarrhoea

Non-inflammatory
eg. Malabsorption
Syndrome

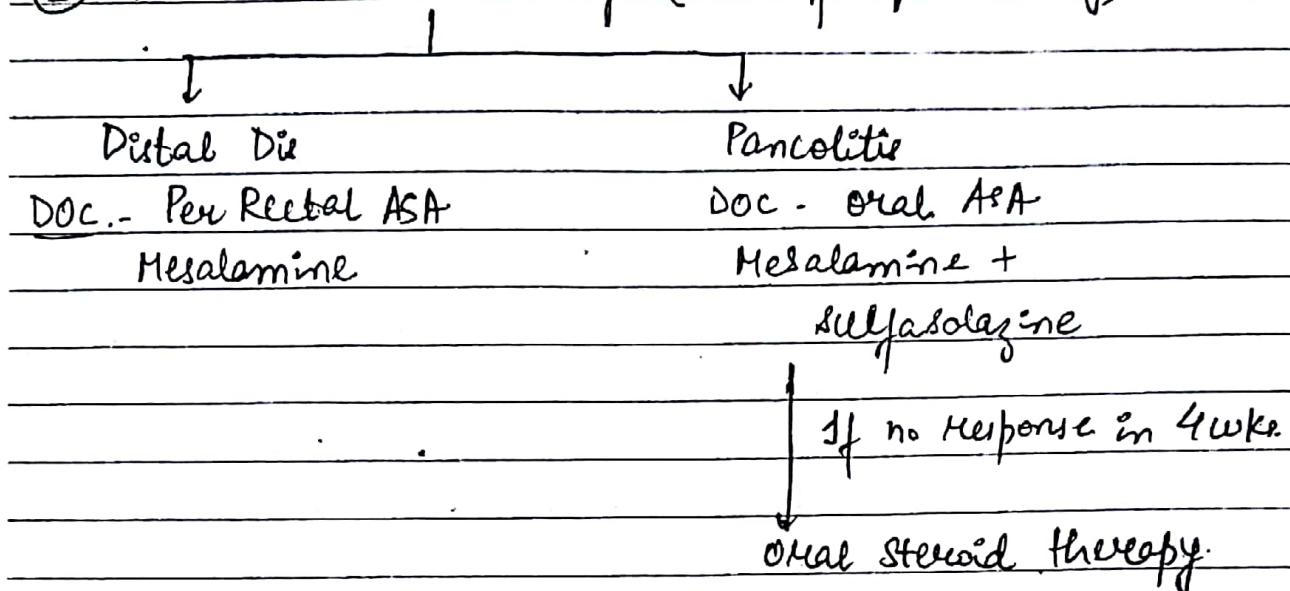
Inflammatory
LHR
Topic (Ulcerative colitis) IBD
(Crohn's Disease)

UC	CD
*Risk/associated	
① Smoking ↓	↑
② appendectomy ↓	↑
③ Drugs	∞
OCP ↔	↑
Methyldopa ↑	↔
Ab use in 1 year ↑	↔
④ Infections ↔	↑ MC = Mycobacterium Paratub. Infection ↓ risk of CD - H. Pylori
⑤ Turner's ↑	↑ NOT DOWN SYNDROME
⑥ IL-10 Receptor deficiency ↑	↑
⑦ anti-inflammatory → Early onset IBD.	
C/F. Intestinal	
M/c site → Rectum + Sigmoid → Rectum only	M/c site → SI + LI > SI only. M/c isolated site - Ileum.
M/c isolated site - Rectum Site not involved → SI.	Rectum is usually spared

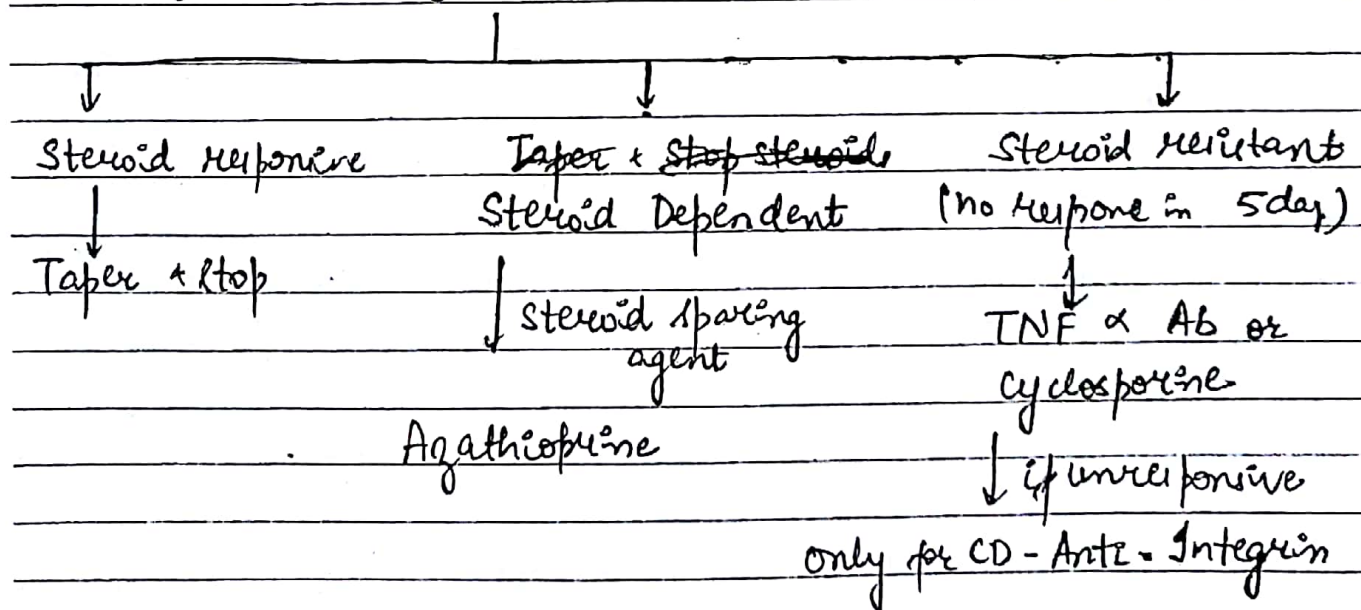
① Malabsorption synd \ominus	\oplus
② Bleeding PR (Tenesmus) \oplus	\ominus
③ Fistula formation \ominus	\oplus (Transmural involvement)
④ Toxic Megacolon. \oplus (dilatation of colon $>6\text{cm}$)	\ominus Bowel wall or thick neist dilatation
Ulcer \rightarrow Collar Button ○ (non-erosing)	Cobblestone ulcer ## (erosing)
Inv	
① Stool Exam ⁿ Lactoferrin \oplus correlate \bar{c} disease activity	\oplus
Calprotectin \oplus Predicts relapse relapse	\oplus
② Serology. H/c \rightarrow ANCA	Hc Anti Sacromyces cerevisae Ab
Role \rightarrow \uparrow risk of Pancolitis	Role - \uparrow risk of early complication
③ Confirm Bx	Bx

Rx of Ulcerative Colitis

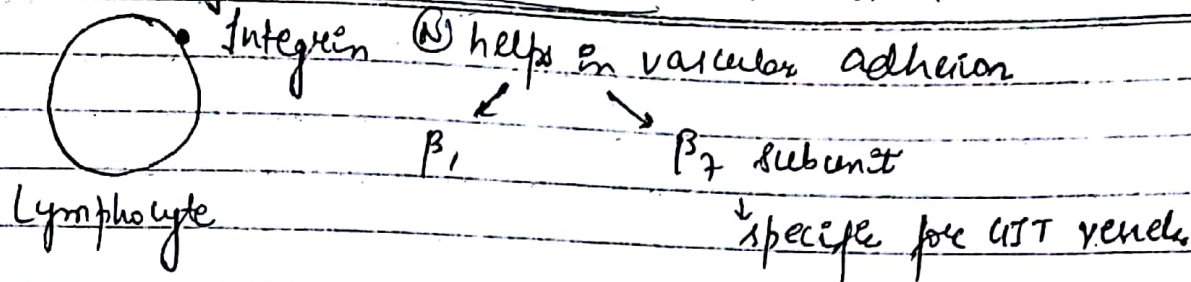
(I) Mild to mod. severity (stool freq. $< 6/\text{day}$)



II Severe IBD (stool frequency $> 6/\text{day}$, or shock).
DOC - I.V. Steroids



Only in Crohn's Disease (Perianal) ^{steroid}



Ab against $\beta_1 + \beta_2 =$ NATALIZUMAB.
(used in Multiple Sclerosis)

\downarrow
S/E \rightarrow Reactivate JC virus

\downarrow
Progressive multifocal
leukoencephalopathy

Ab against $\beta_2 =$ VEDOLIZUMAB

Rx of Crohn's Disease

I. Mild to Mod. IBD

\downarrow

Ileum limited
Doc - Oral Release
Budesonide

\downarrow

Small + Large Intestine
Doc - Oral prednisolone

\downarrow no response in 4wks
Methotrexate.

* Miscellaneous Points :-

1) He cause of death \rightarrow Cancer.

2) Colonic Cancer risk \rightarrow Ulcerative Colitis = Crohn's Disease

3) Colonics Ca risk ↓ → Folic acid, ASA agents.

4) Extraintestinal Manifestation of IBD (usually more in CD)

↓
Correlated to Bowel
activity

Skin - ① Erythema Nodosum
(Red, hot, tender, nodules
on shin)

↓
Independent of Bowel
activity

N - neutrophil infiltration
N - non-infective
N - necrosis of skin.
① Pyoderma Gangrenosum

Joints - Migratory Polyarthritides
(Peripheral joints)

Ankylosing Spondylitis

Eye - Episcleritis

Uveitis

Liver - Non-alcoholic fatty
Liver Disease

Set 1° B Sclerosing Cholangitis
↓
Risk factor for
Cholangio Carcinoma

Q. M/c extra-intestinal organ affected in IBD - Joints.

Q. M/c " " manifestation. → Erythema Nodosum

Q. C " " " more in UC → Pyoderma
1° sclerosing cholangitis

Addition Harrison Selected.

Part I → Involuntary wt. loss - Dejn
 causes
 Inv (Table)

Ascites

Table of causes of diarrhoea

Part II - Table of T/t of Hepatitis C
 (exclude doses or regimen)

Table of intestinal Biopsy findings

Protein losing enteropathy
 (1st 2 para - causes
 Inv)